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Organic phosphorus insecticides may cause mild illnesses in persons working closely with the materials, but they did not constitute any hazard for residents surveyed recently in Wenatchee, Wash.

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Exposure to Organic Phosphorus Sprays and Occurrence of Selected Symptoms

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PESTICIDES are used intensively in agriculture in the vicinity of Wenatchee, Wash. Direct measurement of dermal and respiratory exposure of sprayer operators in this area to parathion was reported by Batchelor and Walker in 1954 (*1*). A survey designed to evaluate the hazard of organic phosphorus insecticides was carried out in this same locality during 1951 (*2*). It was found that definitely exposed persons showed a significant reduction in average cholinesterase values and an increase in illnesses consistent with poisoning during the period of their exposure. There was no evidence of either reduced cholinesterase activity or increased illness during the spray season in persons with little or no exposure to insecticides.

This survey was continued during the 1952 and 1953 seasons. The present paper presents the results of that work.

Dr. Hayes is chief of the Toxicology Section, Technical Development Laboratories, Communicable Disease Center, Public Health Service, Savannah, Ga. Dr. Dixon was stationed at the CDC Wenatchee Field Station, Wenatchee, Wash., when this study was made. He is now at the Kettering Laboratory, University of Cincinnati College of Medicine. Mr. Batchelor was the entomologist for the Wenatchee Field Station, and is now with the Allied Chemical and Dye Corp. in Wenatchee. Dr. Upholt is chief of the Wenatchee Field Station.

Kenneth C. Walker, a chemist at Wenatchee, determined the cholinesterase activity of the blood samples for the study, and Dr. William F. Durham, a biochemist at the CDC laboratories in Savannah, assisted in preparing the report. Dr. J. Monte Johnston and Dr. W. T. Sumerford participated in the early phases of the surveys while they were stationed at Wenatchee.

Materials and Methods

The procedure was essentially the same as that used in the 1951 survey (*2*). The subjects were again grouped according to decreasing potential exposure as follows: mixing-plant personnel (MPP), commercial applicators (CA), part-time applicators (PTA), workers in orchards (WO), fieldmen, warehousemen, and miscellaneous workers (FWM), residents living near orchards (RNO), residents of Wenatchee area living far from orchards (RFO), and a control group of residents living completely outside the agricultural area (ROA).

The four exposure periods were again based on the best information which could be obtained regarding exposure to insecticides for each individual. The observations on the potentially

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exposed groups (RNO and RFO) and the definitely unexposed group (ROA) were divided into periods based on the observed periods of exposure for the exposed groups. The periods were preexposure, exposure, recovery (arbitrarily taken as the 30-day period immediately following the last exposure of the season), and postrecovery. Also included in the recovery period were any data obtained from a person known to be in a convalescent state following poisoning, provided that he avoided further exposure.

In 1952, 228 persons were studied, including 100 of the same subjects studied in 1951. A total of 923 blood samples were analyzed for erythrocyte and 927 for plasma cholinesterase activity, using the electrometric method of Michel (*3*). Two hundred and twenty of the subjects were interviewed periodically for symptoms, as well as history of exposure.

In 1953, 239 persons in four of the groups were studied: commercial applicators (34 persons), residents near orchards (62 persons), residents far from orchards (107 persons), and residents outside the area (38 persons). These groups were selected to represent occupationally exposed (CA), potentially environmentally exposed (RNO and RFO), and definitely unexposed (ROA) populations. Cholinesterase determinations were not carried out on these subjects. In this year an effort was made to achieve greater statistical significance for the survey of symptoms by (*a*) increasing the number of observations in each group and (*b*) equalizing, insofar as possible, the number of observations from the various exposure periods. Most of the participants were interviewed each month, starting in some instances as early as March and extending through November or December. In an effort to assure as much uniformity of sampling as possible between the exposure periods, no individual participant was included in the final tabular summary unless he had been interviewed at least once in each of three periods, including both the preexposure and the exposure periods.

Cholinesterase Values

The results of the cholinesterase activity determinations are given in table 1. The groups with occupational exposure (MPP, CA, PTA, and WO) showed a definite decrease in plasma cholinesterase levels and some diminution in erythrocyte enzyme values during the exposure period. Though the decrease in mean values was not great in any group, it was largest in the group with the heaviest exposure, the mixing-plant personnel. The lowest values (cells, 0.05; plasma, 0.09) encountered during the exposure period were in a person living near an orchard. These extremely depressed cholinesterase activity levels were the result of a near-fatal, acute case of organic phosphorus poisoning suffered by a 2-year-old child who had played with a can from which the original contents of 25 percent emulsifiable parathion concentrate had not been completely removed. The poisoning incidents reported by Johnston (*4*) and Dixon (*5*), as well as several unpublished cases, support the conclusion that, although extensive day-to-day exposure is regularly associated with reduced blood cholinesterase activity, the only fatal and near-fatal cases of poisoning which were found were associated not with long-standing exposure but with brief, massive exposure and gross carelessness.

In the recovery period, the average plasma enzyme values of 3 of the 4 occupationally exposed groups (MPP, PTA, and WO) had returned essentially to their normal levels. The commercial applicators still showed a somewhat depressed average plasma cholinesterase level at this time. For two of the groups with greatest exposure (MPP and CA), the erythrocyte enzyme levels were still significantly subnormal during the recovery period.

Few postrecovery samples were obtained. The values found were all in the expected range except for one low plasma value for a single resident near an orchard. This low plasma value, which was associated with a normal red cell value, must be considered characteristic of the individual in question because it continued low after an appreciable time with no possible exposure.

It is of interest to note that the average preexposure cholinesterase levels of individuals living in an intensively sprayed area are essentially the same as those of individuals living in unsprayed areas. The three less-exposed

Table 1. Cholinesterase values for various occupational and control groups in relation to exposure to organic phosphorus insecticides, Wenatchee, Wash., 1952

Group	Number of people	Number of samples	Cholinesterase values (Δ pH/hour)					
			Red blood cells			Plasma		
			Range	Mean	Standard error	Range	Mean	Standard error
Preexposure period								
MPP	7	11	0.60–0.92	0.73	0.03	0.50–1.18	0.74	0.06
CA	16	28	.61–.81	.70	.01	.66–1.26	.91	.03
PTA	39	49	.57–.90	.71	.01	.40–1.18	.85	.01
WO	14	14	.57–.84	.70	.02	.54–1.12	.83	.04
FWM	12	21	.58–.86	.73	.02	.53–1.36	.90	.04
RNO	21	31	.61–.90	.72	.01	.45–1.17	.80	.04
RFO	12	26	.50–.84	.72	.01	.61–1.02	.85	.01
ROA [1]	14	38	.64–.88	.73	.01	.54–1.28	.92	.04
Exposure period								
MPP	8	24	0.15–0.80	0.62	0.03	0.14–0.81	0.57	0.04
CA	30	84	.21–.92	.64	.03	.14–1.10	.67	.03
PTA	59	[2] 165	.41–.90	.68	.01	.26–1.26	.79	.01
WO	13	[3] 36	.54–.84	.68	.01	.49–1.05	.74	.02
FWM	29	79	.45–.89	.71	.01	.36–1.62	.86	.03
RNO	28	110	.05–.94	.69	.03	.09–1.19	.76	.06
RFO	15	59	.50–.86	.69	.01	.58–1.02	.81	.02
ROA [1]	14	[4] 59	.58–.84	.70	.01	.48–1.27	.90	.03
Recovery period								
MPP	2	2	0.52–0.70	0.60	0.07	0.75–0.81	0.78	0.03
CA	16	22	.09–.86	.53	.05	.05–1.15	.69	.05
PTA	14	[5] 14	.38–.82	.67	.03	.52–1.09	.79	.05
WO	3	3	.62–.72	.69	.20	.59–0.92	.78	.10
FWM	5	5	.61–.82	.72	.04	.46–1.08	.83	.10
RNO	6	7	.18–.80	.55	.09	.26–1.14	.70	.12
RFO	2	2	.71–.74	.72	.02	.96–0.98	.97	.00
ROA [1]	9	9	.60–.86	.73	.04	.59–1.26	.94	.08
Postrecovery period								
MPP								
CA	7	7	0.48–0.90	0.66	0.18	0.68–1.15	0.83	0.06
PTA	4	4	.55–.78	.66	.05	.76–1.02	.92	.07
WO	1	1		.78			.87	
FWM	4	4	.59–.80	.70	.04	.67–1.32	.97	.14
RNO	1	1		.64			.48	
RFO	1	1		.76			.69	
ROA [1]	11	11	.66–.92	.75	.02	.60–1.27	.98	.07

[1] The averages for the year in this group were 0.72 for cells and 0.92 for plasma. Although this group was not exposed to the spray chemicals under investigation, the cholinesterase values were distributed on the basis of collection date to the four periods set up for the exposed groups. This distribution provided a control for any potential seasonal variation in cholinesterase values.

[2] Only 164 red cell values available.

[3] Only 35 red cell values available.

[4] Only 58 red cell values available.

[5] Only 13 red cell values available.

Table 2. Occurrence of illness and of selected symptoms among various occupational and control groups in relation to exposure to organic phosphorus insecticides, Wenatchee, Wash., 1952

Group	Number of people	Number of illnesses	Percent of persons with illness	Percent of observed illnesses exhibiting—																	
				Selected symptoms																At least 1 selected symptom	Myosis or at least 3 other selected symptoms
				Headache	Nausea	Weakness or fatigue	Pain or tightness in chest	Abdominal pain	Vertigo, fainting, or incoordination	Vomiting	Nervousness, drowsiness, or insomnia	Sweating	Cough or expectoration	Disturbance of vision	Loss of appetite	Shortness of breath	Nasal discharge, including postnasal drip	Myosis	Wheeze		
Preexposure period																					
MPP	8	2	25													50		*		50	0
CA	30	13	43	31				8				8	15	8		8	31			62	0
PTA	39	19	53	5	5		11	11					21			5			5	32	5
WO	7	4	57	50										25						75	25
FWM	12	5	41									20		20			20			20	0
RNO	83	77	93	26	4	5	8	3	5	3	21	1	14	5	3	6	40		3	78	16
RFO	119	116	97	30	6	10	8	9	2	4	23	1	22	3	5	3	30		2	76	17
ROA	57	47	82	19	4	4	2	8		2	23		13	2		6	19		2	51	13
Exposure period																					
MPP	8	6	75	17		33	50						50			33		50	50	67	67
CA	68	60	88	52	13	13	33	5	5	2	10	2	23	15	8	15	20	55	18	85	48
PTA	59	48	81	50	25	54	14	12	23	12	19	14	25	12	14	10	10	12	4	75	33
WO	12	7	58	28	28	28			28	14	28	28	71	28	28	14	28		14	71	57
FWM	28	20	75	30	5	20	40	15	15		20	20	25	10	10	25	25	5	15	90	25
RNO	90	90	100	30	6	14	3	3	4	3	22		26	4		3	40	1	6	66	23
RFO	122	117	96	40	8	15	9	12	3	6	26	3	24	2	5	6	43		3	83	27
ROA	59	49	83	12	6	8		12	2	4	18		14	2			26		2	57	12
Recovery period																					
MPP	2	0	0																		
CA	38	22	58	23	55	18	18	9	5	5		9	23	9	5		18	5		73	14
PTA	14	8	57	75	12	50		12	12	25	12	12	25	12		12	12	12		75	25
WO	3	3	100				33						33				67		33	67	67
FWM	5	2	40				50						100				50			100	50
RNO	54	48	89	23	2	10	2	6	4	4	25		12			2	31	2	6	62	15
RFO	98	93	95	11	4	10	3	8		1	12	2	13	1	4	3	24		2	55	11
ROA	49	37	76	11		5		8			8		11				19		3	41	5
Postrecovery period																					
MPP	0	0	0																		
CA	41	21	51	14			5	5			5		24				33			71	0
PTA	4	4	100				25		25				25				25			75	25
WO	1	0	0																		
FWM	4	1	25																	0	0
RNO	63	61	97	26	10	20	2	11	2	10	2		25	2	2		48			66	21
RFO	101	94	93	21	10	14	3	13		7	10		24	2	3	2	50			71	20
ROA	61	54	89	15	13	13	2	13		13	9	2	22		11	2	37			56	22

NOTE: Values are zero unless otherwise indicated.

groups (FWM, RNO, and RFO) as well as the definitely unexposed population (ROA) remained normal during all periods.

Symptomatology

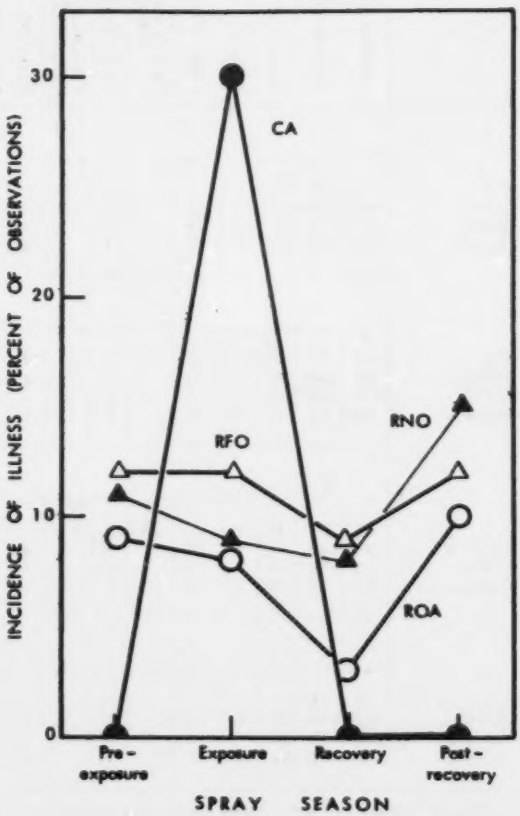
The symptoms recorded during the 1952 survey are tabulated in table 2 in the same form used in the earlier study (*2*). The distribution of the nonspecific symptoms throughout the various groups and throughout the four periods showed no particular pattern. In contrast the selected symptoms listed in the table were noted much more frequently during the exposure period. This finding indicates that mild illnesses involving symptoms similar to those characteristic of organic phosphorus intoxication were significantly increased during the exposure period. However, on the basis of the 1952 survey, as was also true for the 1951 study, it was not possible to differentiate clearly among the various potentially exposed groups with respect to the incidence of this type of illness. In an effort to solve this problem, the protocol of the survey was modified somewhat for 1953, as described above.

The symptoms recorded during the 1953 survey are shown in table 3. In this tabulation the incidence of symptoms and of illnesses is based on the number of observations, not on the number of illnesses or the number of persons as in table 2.

The incidence of all illnesses revealed that the commercial applicators were generally "healthier" than either the environmentally exposed groups or the unexposed group. The unexposed group had a slightly lower incidence of symptoms and of illnesses in all four periods than did the environmentally exposed groups (RNO and RFO). This lower incidence, however, is considered to be unrelated to exposure since these groups were different with respect to their potential contact with insecticides only during the exposure period.

The increase in illnesses among the commercial applicators during the exposure period was a result of an increase during this period in the selected symptoms known to be associated with intoxication by organic phosphorus compounds. The difference between periods was most apparent for the frequency of headache, nausea, pain or tightness in the chest, and myosis. The significance of this trend can be seen by considering the incidence of myosis or of illnesses involving three or more of the other selected symptoms. As explained in the earlier report, the occurrence of myosis or of three or more other selected symptoms is a stronger indication of intoxication from organic phosphorus insecticides than is the occurrence of unselected symptoms or of any single symptom other than myosis. Each of the selected symptoms other than myosis occurs quite commonly as a result of conditions unrelated to exposure to insecticides, but they are not so likely to occur in combination without easily recognized etiology.

Incidence of illness involving myosis or at least three other selected symptoms among groups occupationally exposed (CA), environmentally exposed (RNO and RFO), or unexposed (ROA) to organic phosphorus insecticides, Wenatchee, Wash., 1953.



The incidence of myosis or of three or more of the other selected symptoms is shown in figure 1, as well as in table 3, for each of the groups. Especially in view of the generally lower incidence of symptoms of any kind among the commercial applicators, the great rise in this group in the incidence of illnesses involving myosis or three or more other selected symptoms during the exposure period is striking. Actually, 7 of the 8 illnesses in this group could be clearly correlated with known heavy exposure to either parathion or tetraethyl pyrophosphate. Six of them included myosis as well as two or more other selected symptoms. The eighth case was presumably a respiratory infection that was epidemic at that time.

Since the number of commercial applicators was very small, data for 18 such workers not included in the above analysis because they were missed in the preexposure period were also examined. These 18 were observed in the exposure period and at least once in the recovery or postrecovery periods. As shown in table 4, the inclusion of the observations for

Table 3. Occurrence of illness and of selected symptoms among various occupational and control groups in relation to exposure to organic phosphorus insecticides, Wenatchee, Wash., 1953

Group	Number of people	Number of observations	Percent of observations revealing—																			
			Selected symptoms																Any illness	At least 1 selected symptom	Myosis or at least 3 other selected symptoms
			Headache	Nausea	Weakness or fatigue	Pain or tightness in the chest	Abdominal pain	Vertigo, fainting, or incoordination	Vomiting	Nervousness, drowsiness, or insomnia	Sweating	Cough or expectoration	Disturbance of vision	Loss of appetite	Shortness of breath	Nasal discharge, including postnasal drip	Myosis	Wheeze			
	Preexposure period																				
CA	16	20	15				5					15	5		10	5			70	30	0
RNO	62	108	17	2	3	5	2	2	2	17		12	3	1	6	32		3	98	61	11
RFO	107	178	22	4	8	7	6	2	4	21		18	2	4	2	25		2	97	67	12
ROA	38	56	16	5	7	2	2		4	9		14	2		4	20			82	45	9
	Exposure period																				
CA	16	27	37	11	4	18		4	4	4		7	4		4	22	18	2	81	56	30
RNO	62	159	19	2	6	1	2	3	1	18		15	1		1	26		2	98	57	9
RFO	107	268	23	3	7	4	6	1	2	19		14		3	2	24		1	94	62	12
ROA	38	65	9	5	6		6	2	3	12		8				22			86	42	8
	Recovery period																				
CA	11	11	9			18	9						9			27			91	64	0
RNO	48	48	20	2	8		6	2	2	22		10			2	28		2	88	52	8
RFO	96	96	9	4	7	3	7		1	11	1	13	1	4	3	22		2	95	51	9
ROA	32	32	9		3		6			6		6				16			78	34	3
	Postrecovery period																				
CA	16	26					8					4				15			65	31	0
RNO	62	110	20	6	12		8	1	6	1		17	1	1		35			95	49	15
RFO	100	184	13	5	10	2	7		4	7		15	1	2	2	28			89	49	12
ROA	38	70	11	9	7		7		9	3		10		7		20			84	31	10

NOTE: Values are zero unless otherwise indicated.

Table 4. Occurrence of illness and of selected symptoms among persons occupationally exposed to organic phosphorus insecticides, Wenatchee, Wash., 1953

Item	Exposure period	Recovery period	Postrecovery period
Number of individuals	34	22	34
Number of observations	55	22	51
Percent of observations revealing any illness	87	86	63
Percent of observations revealing at least 1 selected symptom	67	59	33
Percent of observations revealing myosis or at least 3 other selected symptoms	36	5	0

this group with those for the original group increases somewhat the incidence of illnesses involving at least one selected symptom and the incidence of myosis or of at least three other selected symptoms during the exposure period. Thus it strengthens the conclusion that there was a highly significant increase in this type of illness among occupationally exposed individuals during the period of exposure.

The occurrence of three or more selected symptoms was slightly more frequent among the environmentally exposed groups (RNO and RFO) than among the unexposed group (ROA) in all periods. (None of these groups reported myosis.) As suggested above, however, this difference was probably due to uncontrolled variables. Twelve of the eighteen illnesses involving three or more selected symptoms in the unexposed group were fairly definitely associated with etiologies unrelated to intoxication. Ten of the twelve were diagnosed as influenza or upper respiratory infection. One person had an operation for an intestinal obstruction, and another had cardiovascular disease. It is significant that of the 6 illnesses that were not adequately explained, 3 occurred in the preexposure period, 2 in the postrecovery period, and only 1 in the exposure period.

Of the 46 illnesses with three or more selected symptoms (but no myosis) found in the residents near orchards, 35 were fairly clearly associated with etiologies unrelated to insecticide exposure. These included upper respiratory infection, known allergies, pregnancy, peptic ulcer, and scarlet fever. The 11 that were not adequately explained were distributed 3 in the preexposure period, 3 in the exposure period, 1 in the recovery period, and 4 in the postrecovery period.

There were 84 illnesses revealing three or more selected symptoms (but no myosis) among the residents far from orchards; of these illnesses, 42 could be associated with etiologies unrelated to insecticide exposure, including about the same ones as those found in residents near orchards. Of the 42 illnesses that were not adequately explained, 15 occurred in the preexposure period, 16 in the exposure period, 6 in the recovery period, and 5 in the postrecovery period. With such a distribution there would seem to be little, if any, basis for associating these unexplained illnesses with exposure to insecticides.

Summary and Conclusions

A study of the effect of exposure to organic phosphorus insecticides carried out during 1952 and 1953, using some of the same subjects as those observed by Sumerford and his colleagues in 1951 (*2*), confirmed the previously demonstrated relationships between blood cholinesterase levels, exposure, and illness. It also provided further evidence that the occurrence of myosis or three or more other selected symptoms is a criterion for the differential diagnosis of mild poisoning. None of the results of the new investigation contradicted any conclusion stated in the first report.

In addition to these confirmatory findings, the present study showed clearly for the first time that illness resembling mild poisoning was not significantly more common in persons living in an agricultural community who had no occupational or gross accidental exposure than it was in persons living in a nonagricultural area, where insecticides were not used.

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ARTICLES

EXPOSURE OF MOSQUITO CONTROL WORKERS TO FENTHION[1]

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ABSTRACT. Values for potential dermal and respiratory exposure were determined for workers applying fenthion for mosquito control. Application was by hand gun power spray equipment, back-pack hand pressure sprayer and hand granular dispersal. Potential dermal exposure was much greater than potential respiratory exposure. Exposure was found to be greater during hand dispersal of dry granular formulation. Highest total dermal-respiratory exposure for any individual was calculated to be only 0.03% of a toxic dose per hour of work activity. Tests to determine hazard from smoking during application operations indicated greater contamination of cigarettes as a result of contact with unwashed hands following hand granular application than following spray application operations. There was no important change in erythrocyte cholinesterase activity; however, there was some decrease in plasma cholinesterase activity in certain workers.

Fenthion, O,O-Dimethyl O-(4-methylthio)-*m*-tolyl) phosphorothioate, has been used to some extent in the Pacific Northwest for mosquito control during recent years. Because it is more toxic to warm-blooded animals than many of the other compounds used, there has been some concern about hazard to workers who apply the pesticide. Published reports from other countries (Taylor 1963, Elliott and Barnes 1963) have stated that use of this pesticide as a residual spray in mosquito control operations has produced moderate depression of whole blood and plasma cholinesterase in spraymen and in inhabitants of sprayed dwellings.

During the last several years we have analyzed many blood samples from workers in mosquito abatement districts who had been exposed to fenthion. During this period we received several inquiries as to the potential health hazard from working with such a compound. Because of this interest we made observations of application practices and conducted the present studies to determine the potential exposure to fenthion during field application operations.

MATERIALS AND METHODS. Studies of potential dermal and respiratory exposure to fenthion involved measurement of exposure during application of 0.06% spray or hand dispersal of the 1% granular formulation. Of 33 different work periods studied over two work seasons, 12 were during operation of hand gun power spray equipment, 10 were during back-pack hand pressure sprayer operation, and 11 were during granular dispersal. Estimation of the amounts of dermal and respiratory exposure to which the workers would potentially be subjected followed the exposure pad and hand rinse techniques and procedures described by Durham and Wolfe (1962). Potential dermal contamination was measured primarily by attaching absorbent *a*-cellulose pads for spray exposure, or layered gauze pads for dry formulation exposure, to various parts of the worker's body or clothing and allowing them to be exposed during a timed period of work. However, dermal contamination of hands was measured by use of the bag rinse technique using 95% ethyl alcohol as the solvent. The amount of pesticide entering the body via the respiratory route was estimated from the contamination of special filter pads held in single-unit respirators worn by the subjects. The filter pads were covered with inverted plastic funnels modified to a specific aperture size to re-

[1] From the Field Studies Section, Pesticides and Toxic Substances Effects Laboratory, U.S. Environmental Protection Agency, P.O. Box 219, Wenatchee, Wash. 98801.

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produce as nearly as possible the aerodynamics of air flow through the nostrils. The funnels also prevented direct impingement of spray droplets or particles onto the pad except for those carried through the apertures by respiratory action. This technique renders it unnecessary to measure total air volume because all inhaled air passes through the filter pads.

We have noticed that mosquito control workers often smoke cigarettes while applying spray or dispersing granules. To obtain information that might be useful in estimating potential health hazard from smoking during application operations, workers who did not wear gloves were given cigarettes to be exposed during their regular work activities. Near the end of a full work day they were allowed to remove a test cigarette from a package, light it, and smoke it to one-half the total length. The remaining portion was then analyzed to determine the amount of pesticide that had been imparted to the cigarette as a result of contact with the worker's hands.

In order that exposure estimations be based on the safe side, the total amount of fenthion found on and in the analyzed portion of a cigarette was considered to be the amount of potential exposure from smoking the cigarette. This is based on the assumption that the pesticide would be volatilized and drawn through the cigarette, and that none of the volatile or particulate pesticide would be lost into the air, broken down by burning, or trapped in the butt end or filter of the cigarette. However, all of these factors are undoubtedly involved, so one would expect the amount of pesticide actually drawn through a cigarette to be considerably less than the total amount on and in the cigarette.

A study of blood cholinesterase levels was made on 9 workers during one work season and 8 workers during another season. As many of each group as possible were checked at the pre-exposure period and at approximately monthly intervals for 4 samplings during the work season. Workers during the first season study occasionally used compounds less toxic than fenthion, so their total exposure to that compound was less than that of the second season workers who were involved in more intensive and exclusive use of fenthion.

Chemical analysis of samples for fenthion was by electron-capture gas-liquid chromotography. Blood cholinesterase activity determinations were carried out by the electrometric method of Michel (1949).

RESULTS AND DISCUSSION. As can be seen in Table 1, calculated potential exposure values for workers during operation of power sprayers or back pack hand pressure sprayers were approximately the same. During hand granular dispersal the values were over 3 times greater than those for spraying activities. Mean dermal and

TABLE 1. Potential dermal and respiratory exposure of mosquito control workers to fenthion during three types of application.[a]

Method of application	Route of exposure	Exposure situations studied	Exposure (mg/hr)	
			Range	Mean
Power sprayer [b]	Dermal	12	0.1–11.4	3.6
	Respiratory	11	<0.001[d]–0.092	<0.016
Hand pressure sprayer [b]	Dermal	10	0.1–6.3	3.6
	Respiratory	6	<0.001[d]–0.067	<0.021
Hand granular dispersal [c]	Dermal	11	2.8–58.8	12.3
	Respiratory	10	0.004–0.186	0.088

[a] Calculated on the basis of the worker wearing a short-sleeved, open-necked shirt, no gloves or hat, and with his clothing giving protection of the areas covered.
[b] 0.06% spray.
[c] 1% granular material.
[d] Below lower limit of sensitivity of test.

respiratory exposure values during operation of power sprayers were 3.6 and <0.016 mg/hr of work, respectively, and for hand pressure sprayer operators the values were 3.6 and <0.021, respectively. Mean dermal exposure value for hand granular dispersal was 12.3 mg/hr and for exposure via the respiratory route the mean value was 0.088 mg/hr of work activity. In all three operations the unprotected body parts subjected to the greatest exposure were the hands, with only slightly less on the forearms. The combined hand and forearm exposure in the three types of application was from 73.9 to 87.5% of the total potential exposure to all exposed body parts. We believe this indicates that exposure as a result of direct hand and forearm contact with the pesticide formulations or with pesticide-contaminated equipment was probably a more important factor in total dermal exposure than was exposure from drift of spray droplets or dust from granules. Dust from the granular formulation was undoubtedly an important factor in respiratory exposure.

A wide range of potential exposure in different work periods or situations can be seen. However, the individual with the greatest potential exposure (58.8 mg/hr dermal and 0.186 mg/hr respiratory during hand granular dispersal) would be subjected to only 0.03% of a toxic dose of fenthion per hour of work as calculated by the method of Durham and Wolfe (1962). This maximum exposure level would probably rarely be maintained throughout a full work day considering the variation in values obtained.

Results of cigarette contamination tests in 18 different exposure periods involving workers applying spray by power machine or back-pack pressure hand sprayer showed contamination values from 3.2 to 78.5 micrograms of fenthion per cigarette with a mean of 28.3 micrograms. In 10 exposure periods involving workers dispersing dry granular fenthion, contamination was much greater, ranging from 137.2 to 233.0 micrograms of fenthion per cigarette with a mean of 161.4 micrograms. The reason for greater contamination of cigarettes during granular dispersal operations is not known for sure. However, we feel that one factor may be that workers tend to avoid excess exposure of hands to the dilute and concentrate liquid spray materials; whereas, in hand dispersal they deliberately handle the material with bare hands and thus build up more fenthion on the skin even though the granular formulation may be less concentrated than some of the liquid contacted. Also, dry particulate material from the granules is more dislodgeable from the hands and, if much of the material is transferred to the cigarette surface, this could be a factor in producing more contamination.

In a study of blood cholinesterase levels in 9 workers during a work season where other less toxic compounds, as well as fenthion, were included in the program, no significant effect on either the erythrocyte or plasma cholinesterase levels was found. During another work season where workers were subjected to more intensive and exclusive use of fenthion, a study of 8 workers showed no important change in the erythrocyte cholinesterase activity; however, plasma cholinesterase activity level did show a progressive decrease over the season, reaching the lowest level on August 9 (Table 2). Spraying operations became less active later in the summer and on August 29 there was some recovery in plasma enzyme levels. Among the workers there appeared to be good correlation between magnitude of cholinesterase decrease and apparent exposure to fenthion. Although not shown in the table, changes in plasma cholinesterase were more evident when only the more heavily exposed individuals were considered. At the August 9 sampling, 4 spraymen with heaviest exposure had a mean plasma cholinesterase level of 0.44 ΔpH/hr, representing 52% of the pre-exposure value while 5 men with intermediate or low exposure had a mean level of 0.74 ΔpH/hr (78% of the preseason level). Three employees who spent most of their time in the office and laboratory showed no important variation

TABLE 2. Mean erythrocyte and plasma cholinesterase activity levels for mosquito control workers exposed to fenthion.

Period	Date	No. of subjects		Cholinesterase activity (ΔpH/hr) Erythrocytes	Plasma
Pre-exposure	June 6	7	Range	0.45 – 0.97	0.45 – 1.25
			Mean±S.E.*	0.57±0.07	0.90±0.09
Exposure I	June 21	8	Range	0.56 – 0.83	0.39 – 1.10
			Mean±S.E.	0.67±0.03	0.75±0.08
Exposure II	July 11	6	Range	0.62 – 0.72	0.62 – 0.99
			Mean±S.E.	0.66±0.01	0.77±0.06
Exposure III	August 9	8	Range	0.61 – 0.81	0.15 – 0.99
			Mean±S.E.	0.70±0.02	0.59±0.09
Exposure IV	August 29	7	Range	0.43 – 0.75	0.49 – 1.04
			Mean±S.E.	0.57±0.06	0.68±0.09

* Standard error of the mean.

in cholinesterase level over the season. The lowest plasma cholinesterase levels were in 2 spraymen who had values of 0.15 and 0.37 ΔpH/hr, respectively, on August 9.

Lower plasma cholinesterase values in certain of these workers, although an indication of absorption of the pesticide, are not necessarily an indication of imminent hazard. We are not aware of any published records of poisoning symptoms in workers whose plasma value was lowered as long as the erythrocyte cholinesterase level remained in the normal range. Poisoning symptoms are more closely associated with erythrocyte cholinesterase level; thus, in this study the important point is that the erythrocyte cholinesterase levels were not significantly lowered. Workers whose plasma cholinesterase activity is found to be appreciably lowered, even though the erythrocyte level is in the normal range, should be observed for any work habits that might be causing excess exposure. They should be advised to be more careful in taking precautions to prevent such exposure. Although intensive study was not made of the health status of the men in this study, no illness or absence from work associated with their pesticide exposure was reported.

Results of the exposure tests do not indicate any appreciable hazard to workers applying fenthion for mosquito control under conditions of the present study. Nevertheless, in light of the lowered plasma cholinesterase values, efforts to keep exposure to a minimum should be maintained. The finding that the hands and forearms are subjected to the greatest amount of contamination indicates that efforts to prevent exposure in those areas could result in appreciable reduction of total exposure. Gloves should be worn whenever possible during application of fenthion. In recommending use of gloves, however, it is important to keep both the hands and the inside of the gloves as uncontaminated as possible, because covering of contaminated skin by impermeable protective material may create conditions which lead to increased absorption.

We have observed that some type of protective gloves are usually worn by spraymen but not by workers dispersing granules by hand. We understand that it is difficult to disperse properly the granular form of the pesticide while wearing any type of glove. Thus, where feasible, consideration should be given to the use of some type of dispersal mechanism which reduces direct hand contact with the pesticide. It is especially important to avoid direct hand contact if the hands have cuts or abrasions which allow a more direct route of entry into the blood stream.

Statements on the pesticide container

label concerning the need for washing pesticide-contaminated hands before smoking or eating offer sound advice. Heeding such advice is especially important following hand granular dispersal operations. Even though values for potential exposure through smoking fenthion-contaminated cigarettes may not appear to reflect any great hazard, two important points must be kept in mind: (1) Pesticide entering by the respiratory route is practically 100% absorbed, and (2) There is no assurance that a more toxic breakdown product will not be formed and inhaled as the high temperature of a burning cigarette reaches the contaminated areas rather than complete destruction of the compound by burning. If a pack of 20 cigarettes is smoked per day and all are contaminated with the maximum value of 233.0 μg per cigarette found in this study during granular application, the worker would theoretically be subjected to 4.7 mg of fenthion per day if all of the contamination was inhaled and absorbed. When this is added to the highest dermal and respiratory exposure values for an 8-hour work day, the combined potential exposure is 476.7 mg per day. Using the method of Durham and Wolfe (1962) to calculate the percent of toxic dose this represents for a 70 kg man, we find that, using the highest exposure values found in the study, a worker would be subjected to only 2.3% of a toxic dose per day. This low value reflects the history of no acute illnesses and minimal effect on blood cholinesterase in mosquito control workers in the Pacific Northwest.

It must be kept in mind that the relatively low exposure values obtained in this study are a result of what might be considered normal operations, and that excess exposure resulting from accidents, such as spillage of the emulsifiable concentrate formulation on the skin, could result in enough absorption to cause acute poisoning. In case of accidental gross contamination of skin, every effort should be made to cleanse the contaminated area as quickly and thoroughly as possible. The best recommendation at present is the use of plenty of soap and water. Wash by rubbing with the hands or with a piece of cloth. Do not scrub with a brush because the outer protective layer of the skin may be abraded enough to allow more rapid absorption of any pesticide not removed. A bar of soap, towel, and container of water for use in washing should be carried on every pesticide application machine or transportation vehicle in case a spillage should occur. If pesticide gets in the eyes they should be thoroughly flushed with water for at least 5 minutes. If a person should feel ill while working with fenthion he should stop work at once and get medical attention. If his illness is diagnosed as being caused by the pesticide, he should not return to work until a physician advises that it is safe to do so.

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Pesticide Exposure From Concentrate Spraying

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THE APPLICATION of pesticidal chemicals in the form of low-volume concentrate spray is receiving increasing attention from entomologists and others concerned with control of insects and other pests of agricultural and public health importance. It is claimed that concentrate spraying has a number of advantages, including lower cost, greater speed of application, and increased effectiveness, as compared to the older, conventional, high-volume dilute spray methods.[1]

One main area of interest with respect to concentrate spraying of pesticides has been in application to fruit orchards. It has been shown that orchard spraymen using the conventional dilute high-volume equipment receive heavier exposure than do applicators spraying row crops, apparently because the air-blast spray equipment used in orchards directs the spray upward into the trees, rather than downward as in the case of row crop spraying with a resultant greater contamination of the operator.[2] Therefore, it has seemed advisable to study the exposure hazards which concentrate spraying might present to the orchard sprayman.

The conventional dilute spray machines employ a large volume of formulation (usually 400 to 1,000 gal per acre), thoroughly drenching the trees until the spray runs off the foliage. The concentrate machines most commonly used in fruit orchards dispense liquid spray that is 8 to 12 times the concentration (8X to 12X) of the conventional dilute spray mixture (1X) and is applied at correspondingly lower gallonage per acre. The low-volume concentrate spray moistens the foliage but does not accumulate to the point of run-off. Spray dilutions intermediate between these extremes are sometimes utilized and are generally referred to as semiconcentrate sprays. The various concentrate ground machines now in use dispense about the same amount of actual pesticide per acre as does the conventional high-volume equipment.

The concentrate droplets are smaller (usually 20μ to 100μ diameter) than those produced by the conventional spray machine (usually over 150μ diameter).[1,3] The mist produced by the concentrate machine is so fine that it is barely visible during spray operations.

The most recent development in concentrate spraying involves equipment which dispenses undiluted technical liquid pesticide.[4] This undiluted low-volume spray has to date been limited to use with aerial application of malathion although research is now going forward on extension of the method to other compounds and to use with ground application equipment. The usual formulation for undiluted low-volume spraying contains around 95% malathion and is about 1,600 times as concentrated (1,600X) as the ordinary malathion formulation used for high-volume air-blast orchard spraying. This newer equipment dispenses spray droplets near 100μ in diameter. Thus, the newer type dispenses more uniform-sized spray droplets.

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Data on spray concentration, application rates, and droplet sizes for the various types of spray applications referred to in the present paper is summarized in Table 1.

The present paper compares the exposure to parathion of orchard spraymen operating concentrate machines with that of workers using the conventional high-volume sprayers.

Materials and Methods

The concentrate spray machines studied dispensed parathion formulations at concentrations from 8X to 12X (0.24% to 0.36%). The conventional dilute machines surveyed dispensed parathion in a 1X (0.03%) formulation.

Estimation of exposure of the spraymen was done using the techniques and procedures described in detail by Durham and Wolfe.[6] Potential dermal contamination was measured primarily by attaching absorbent α-cellulose pads to various parts of the worker's body or clothing and allowing them to be exposed during a period of spray operations. The amount of pesticide contaminating a pad was assumed to be the amount that would contaminate the same area of exposed skin. Exposure of unprotected skin area was calculated from these unit area contamination levels using Berkow's[9] values for surface area of the various body parts. Contamination of hands was measured either by rinsing with ethyl alcohol in a polyethylene bag or by swabbing with alcohol-impregnated gauze swabs.

The total body burden of dermal exposure was calculated on the basis of the exposed person's wearing a short-sleeved, open-necked shirt, no gloves or hat, with his clothing giving complete protection of the areas covered. The average sprayman may often wear more clothing than this. However, recommendations based on exposure values calculated from the lesser amount of protective clothing would tend to be on the conservative side.

Respiratory exposure was estimated from the contamination of filter pads in special single- or double-unit respirators designed to prevent direct impingement of spray droplets onto the respirator pads. The amount of pesticide which was drawn into the respirator with enough velocity to reach the pad was considered to represent respiratory exposure, because it probably would have reached the lungs or at least the nasopharynx. These pads primarily trap particulate matter; thus, it may be that some or all of the parathion vapor present was lost. However, previous work has shown that respiratory exposure values determined by the respirator pad technique and those obtained from air concentration values agree rather closely.[6]

All exposure pads were extracted with ethyl alcohol in a Soxhlet apparatus and analyzed for parathion by the method of Averell and Norris.[7]

The work presented here involved study of 37 different exposure situations and chemical analysis of 239 samples associated with concentrate spraying, and of 67 exposure situations and 505 analyses associated with conventional high-volume spraying.

Results and Comment

The results of dermal and respiratory exposure studies with concentrate spray machines are presented in Table 2. The average calculated potential dermal contamination with parathion was found to be 27.9 mg/hr of exposure. The potential respiratory exposure was calculated to be 0.055 mg/hr.

The results of dermal and respiratory exposure studies with conventional dilute airblast spray machines are presented in Table 3 for comparison. These values are similar to those published earlier from this laboratory[5,8] but represent more recent unpublished work. The average potential dermal contamination with the high-volume equipment was found to be 19.4 mg/hr of exposure. The potential respiratory exposure was calculated to be 0.020 mg/hr.

Thus, the potential dermal exposure appears to be somewhat greater for the concentrate than for the dilute type of equipment. The difference in dermal exposure between the two types of equipment is essentially all contributed by the markedly higher

TABLE 1.—*Summary of Characteristics for Types of Orchard Spray Applications Under Discussion*

Type of Application	Compound	Concentration of Active Ingredient (%)	Relation to Conventional Dilute Spray	Gallons Liquid Spray per Acre	Approximate Droplet Size (Diam in Microns)
Conventional dilute	Parathion	0.03	1X	400-1,000	>150
Semiconcentrate	Parathion	0.05-0.09	1.5X- 3X	100- 400	>150
Concentrate	Parathion	0.24-0.36	8X-12X	15- 100	20-100
Undiluted low-volume concentrate *	Malathion	95	1,600X	0.063	100

* This method has not yet been used in orchards but is included here for comparative purposes.

TABLE 2.—*Potential Dermal and Respiratory Exposure to Parathion While Spraying Orchards With Concentrate (8X to 12X) Air-Blast Equipment*

Body Part	Pad Location or Area Rinsed	No. of Samples	Body Part Area (Sq Ft)	Parathion Recovery (Mg/Sq Ft/Hr)	Calculated Exposure (Mg/Body Part/Hr)
Face	Shoulders	69	0.70	6.3	4.4
Front of neck "V" of chest	"V" of chest	36	0.16	3.4	0.5
Back of neck	Back of neck	37	0.12	5.8	0.7
Forearms	Forearms	71	1.30	6.4	8.3
Hands	Hands	26	0.87	—*	14.0
Total dermal exposure	—	239	3.15	—	27.9
Respiratory exposure	Respirator	25	—	—	0.055

* Rinse of total hand area.

level (3.5 times as great) of hand contamination during spraying with the concentrate machines. It is reasonable that greater contamination of the hands would occur with this type of equipment where contact is with a more concentrated formulation. Observations indicate that hand contamination is common during the filling or loading operation. Most spray machine operators take care to avoid contact with the undiluted concentrate pesticide being poured into the tank but, on the other hand, many make little effort to avoid contaminating their hands with the mixed spray.

As might be expected, contamination of spraymen's hands was found to be directly related to the concentration of the mixed spray being used. Measurement of hand contamination of spraymen operating machines using different concentrations of parathion showed hand exposure of 3.9 mg/hr for the conventional dilute spray machines (1X), 5.5 mg/hr with 1.5 times the conventional concentration (1.5X), 7.0 mg/hr at 3X, and 14.0 mg/hr in the range of 8X to 12X.

The presence of a significant quantity of toxic pesticide on the hands must be considered a potential hazard to the health of the sprayman. The hands often receive cuts and abrasions which might serve to increase the normal rate of absorption through the skin. Also, unless the sprayman is careful to thoroughly wash his hands before eating or smoking, he might transfer some of the pesticide to his mouth.

Exclusive of the hands, dermal exposure was about the same for concentrate (13.9 mg/hr) as for high-volume spraymen (15.5 mg/hr).

There is one additional item relative to a possible increased skin contamination hazard from concentrate spraying which was evident from observation of the spray operations, although it was not detectable in the exposure tests carried out. The wetness of the spray from the concentrate machine and from the high-volume equipment was quite different. Thus, drift from the conventional dilute machine can easily wet the skin or soak through thin layers of clothing because of the relatively large amount of water carrier. However, spray drift from the concentrate machine is so fine and has such a small amount of water carrier that, under most conditions, it dries practically on impact or shortly thereafter. This process usually results in a visible build-up of solid particulate material on the skin or clothing. If a sprayman's clothing rarely or never becomes wet, he may assume that it has not become significantly contaminated and be tempted to wear it for a long period of time without a change to clean uncontaminated clothing. However, after a sufficient quantity of the dry concentrated spray material has built up on clothing, it may penetrate or "dust through" and contaminate the underlying clothing or the skin.

Comparison of Tables 2 and 3 shows that the calculated respiratory exposure for workers operating concentrate machines is approximately 2.7 times as great as for those operating conventional high-volume dilute machines. This difference could very well be the most important factor to consider in evaluating differences in exposure between the two application methods. The greater potential respiratory exposure from concen-

TABLE 3.—*Potential Dermal and Respiratory Exposure to Parathion While Spraying Orchards With High-Volume Dilute (1X) Air-Blast Equipment*

Body Part	Pad Location or Area Rinsed	No. of Samples	Body Part Area (Sq Ft)	Parathion Recovery (Mg/Sq Ft/Hr)	Calculated Exposure (Mg/Body Part/Hr)
Face	Shoulders	134	0.70	7.0	4.9
Front of neck "V" of chest	"V" of chest	65	0.16	2.6	0.4
Back of neck	Back of neck	62	0.12	5.7	0.7
Forearms	Forearms	131	1.30	7.3	9.5
Hands	Hands	113	0.87	—*	3.9
Total dermal exposure	—	505	3.15	—	19.4
Respiratory exposure	Respirator	12	—	—	0.020

* Rinse of total hand area.

trate machines probably is due to the fact that the smaller spray droplets produced by the concentrate machines tend to remain suspended in the air longer and thus present a greater opportunity to be inhaled. Also, the path of the smaller droplets is more easily changed by the influx of air into the nose; thus, these particles tend to be more easily inhaled than large droplets.

It is interesting to note that Braid and his colleagues [9] found lower concentrations of parathion in the breathing zone of operators using semiconcentrate equipment than for workers applying a dilute formulation. However, this comparison seems to suffer from the fact that the semiconcentrate formulation was dispensed by air-blast machine while the dilute spray was applied by handgun. The authors concluded that the apparently reduced hazard with concentrate sprays at the dilutions they studied was more likely related simply to the distance between spray nozzle and operator (12-15 feet horizontally with concentrate and 2-4 feet horizontally and vertically with dilute applied by hand) than to physical differences between the two types of spray particles.

One additional bit of evidence was also obtained in the present study which indicated that the respiratory route was a particularly important source of absorbed parathion for the concentrate sprayman. Thus, study of the pattern of excretion of P-nitrophenol by a sprayman applying parathion (8X) with a concentrate machine was qualitatively similar to that for workers using the conventional equipment. However, excretion of this metabolite tended to reach higher peak levels and to decrease more rapidly following concentrate than after high-volume spraying. Similar quantitative differences in the P-nitrophenol excretion pattern have been noted between oral and dermal exposure of workmen to parathion.[10]

Although there have been numerous instances of cholinesterase depletion and some cases of parathion poisoning in spraymen operating conventional dilute machines,[11-14] no enzyme depletions or exposure-related illnesses in operators of the concentrate machines have been reported to date. Braid and his associates [9] did report illnesses in spraymen using parathion in a semiconcentrate type of equipment which dispensed parathion spray at concentrations of 2X to 3X, although in each of these instances which was investigated it was found that some gross exposure to parathion occurred as a result of negligence. However, the absence of poisoning with machines employing formulations of 8X to 12X or greater is not necessarily an indication that there is less hazard involved with the concentrate machines. There are a number of modifying factors which need to be considered in this regard. First of all, the use of concentrate machines is still somewhat limited. Then, there have also been fewer illnesses involving the conventional dilute machines in the last few years. This improved safety record may be a reflection of the fact that somewhat less parathion has been used in orchards in recent years. And finally, we have observed that operators tend to be more careful to wear respirators during the operation of concentrate machines than while using the conventional dilute machines.

Results from the present study appear to warrant three safety recommendations: (1) Workers operating concentrate spray machines should be especially careful to avoid contamination of the hands with the stronger formulation dispensed by this type of equipment. Such contamination is particularly hazardous if the hands have cuts or abrasions which might increase the absorption rate. Also, oral exposure might follow eating or smoking with contaminated hands. Contamination of hands might be reduced by wearing gloves if care is taken not to allow them to become contaminated on the inside. (2) Because of the greater potential respiratory exposure during concentrate spray operations, workers should be particularly careful to wear an approved respirator while spraying toxic pesticides. (3) Workers operating the concentrate machines should be aware of the contamination of clothing, even though the clothing does not become wet with spray.

The results of the present exposure study indicate that concentrate spraying can be done safely provided that recommended precautions are followed. The good safety record of concentrate sprays during limited use to date corroborates this conclusion.

Summary

Exposure to parathion of orchard spraymen operating concentrate (8X to 12X) air-blast spray machines has been compared with that of spraymen using conventional dilute (1X) air-blast spray machines. The calculated potential dermal exposure for operators of concentrate spray equipment was 27.9 mg/hr as compared to 19.4 mg/hr with the high-volume equipment. The greater dermal exposure with the concentrate machine is primarily due to greater contamination of the hands. Potential respiratory exposure with the concentrate machine was 0.055 mg/hr of exposure, or about 2.7 times that determined for operators of conventional dilute machines (0.020 mg/hr). This greater respiratory exposure for operators of concentrate machines may be due to the greater probability of inhaling the smaller spray droplets produced by that type of machine.

The results of the present study, as well as the good safety record of concentrate sprays, indicate that these techniques can be used safely provided that recommended precautions are followed.

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THE ROLE OF SOCIAL CLASS IN HUMAN PESTICIDE POLLUTION[1]

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Davies, J. E., W. F. Edmundson, A. Raffonelli, J. C. Cassady and C. Morgade (Community Studies, State Div. of Health, 1390 N.W. 14th Ave, Miami, Fla. 33125). The role of social class in human pesticide pollution. *Am J Epidemiol* 96: 334–341, 1972.—In previous pesticide residue surveys of the United States population, residues of *p,p'*-DDT and *p,p'*-DDE have been shown to be higher in blacks than in whites. The role of social class factors in this difference is explored in this paper. In a population survey of 800 residents of Dade County, classified by the Hollingshead Two Factor Index, serum levels of DDT and DDE were significantly lower in the more affluent Social Classes I & II than they were in the less affluent Social Classes IV & V in both races. Within these social classes, blacks still had higher residues. Residues were greater in the less affluent whether classified by the Hollingshead Two Factor Index, census tract population density or median income of the census tract. Significant correlations of DDT and DDE were also observed in the first two decades of life—the approximate DDT age of society. The epidemiologic and public health consequences of these findings, reflective of a tropical clime, are discussed and the role of the domestic environment and the implication for global monitoring studies reviewed.

DDT prevalences; pesticides, human monitoring; social class; socioeconomic factors

INTRODUCTION

In the general population the human pesticide residue whether in fat or blood, is a measure of incidental exposure to the several environmental sources of pesticides. Insofar as DDT (dichloro-diphenyl-trichloroethane) is concerned, residues of *p,p'*-DDT in blood are reflective of recent exposure whereas DDE, the major metabolite of DDT, is more indicative of life-long exposure.[2] Residue surveys of this pesticide in the general population indicate that this pesticide is not homogeneously distributed throughout the population, succinct geographic and demographic differences being recognized. One of the most challenging differences in frequency distribution of DDT residues noted in the United States general population is associated with race. In all recent general population surveys, the mean levels of DDT and its metabolites were greater in blacks than in whites (1–3). A

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[2] All references to DDT and DDE are to the *p,p'*-isomers.

DDT: 2,2-bis (*p*-chlorophenyl) 1,1,1-trichloroethane.

DDE: 2,2-bis (*p*-chlorophenyl) 1,1-dichloroethylene.

Dieldrin: Not less than 85% of 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-endo-exo-5,8-dimethanonaphthalene.

possible explanation for this finding is that the differences are associated with factors relating to the socioeconomic variables.

This paper presents organochlorine residue prevalences from the general population, residents of Dade County, Florida and explores the association of these residues acquired by persons living in this semitropical setting with several socioeconomic variables.

Materials and methods

An organochlorine serologic survey was conducted in a sample of the general population of Dade County, having by interrogation no recent or remote history of having been occupationally exposed to pesticides. Specimens were obtained from visitors to a health and ecology fair, physicians and students in the University of Miami School of Medicine, the custodial staff of the Dade County jail, and persons attending the Dade County Health Card Clinic for serologic clearance for food handling, premarital tests and other diagnostic purposes. Additional specimens were collected from employees of the Dade County School Board, the staffs of the Dade County Health Department and the Office of Equal Opportunity Program. The 581 adults 20 years of age and over included physicians, teachers, business executives, clerks, secretaries, cooks, cleaners, caterers, skilled and unskilled workers and custodial staff. Additional serum specimens were obtained from children and adolescents; 43 were 0–9 years of age and 176 were 10–19 years of age. Social classes were measured by the Hollingshead Two Factor Index (4) which combined the weighted strength of the occupation of the head of the household and his level of education. Thus, professionals were listed in Classes I and II and semiskilled and unskilled workers in Classes IV and V. Information on place of residence in Dade County was obtained and the representativeness of the social profile of the sample was based upon a comparison of the frequency distribution of the male participants according to the median income of census tracts wherein they resided with the frequency distribution of Dade County census tracts classified as to median income. Census tracts were divided into five classes according to median income: Group I—6,000+, Group II—$5,000–5,999, Group III—$4,000–4,999, Group IV—$3,000–3,999, and Group V—<$3,000. Information on the population density of the census tracts was used as an additional measure of the social profile of the male participants. This compaction index was used to classify census tracts into five groups, with high rise apartment census tract areas excluded: Group I —<20 persons per acre, Group II—20–30 persons per acre, Group III—31–40 persons per acre, Group IV—41–50 persons per acre, and Group V—51–60 persons per acre.

Eight cc of blood were obtained from each participant in 10 ml B-D Vacutainer tubes (Becton-Dickenson Co., Rutherford, N.J.). After clotting, the blood was centrifuged and the serum separated and stored at 4 C. Later, specimens were analyzed for organochlorine residues by electron capture gas chromatography. A modification of the Dale, Curley, Cueto method (5) for organochlorine residue analysis in serum was used. The modification involved the use of a rotary shaker which rotated the mixture for a period of two hours. The lower limits of sensitivity for this modified method were 1 ppb (parts per billion) for *p,p'*-DDE, β-BHC, heptachlor epoxide, and dieldrin, and 2 ppb for *o,p'*-DDT, *p,p'*-DDT, *p,p'*-DDD (TDE (tetrachloro-diphenyl-ethane)), respectively. Only serum residues of *p,p'*-DDT, *p,p'*-DDE and dieldrin are discussed in this paper.

Results

Table 1 lists the demographic distribution characteristics by social class of 800 samples collected from Dade County residents. There were 636 males and 164 females, and 497 were white and 303 were black.

Earlier general population pesticide residue surveys had suggested that prevalences

TABLE 1

Demographic distribution of 800 residents of Dade County, Florida general population, by social class, sampled for serum residues of organochlorine pesticides, 1970–1971

Social Class*	No. of residents in social classes by age group (years) and sex																	
	Age: 0–9		10–19		20–29		30–39		40–49		50–59		60–69		70–79		80–89		Total
	M	*F*	*M*	*F*	*M*	*F*	*M*	*F*	*M*	*F*	*M*	*F*	*M*	*F*	*M*	*F*	*M*	*F*	
Whites:																			
I & II	5	2	11	9	34	17	26	9	25	16	19	11	4	3	0	2	1	0	194
III	3	5	19	1	23	4	3	4	3	2	3	3	0	1	0	0	0	0	74
IV & V	13	7	42	3	51	3	29	2	29	5	25	5	7	3	2	3	0	0	229
Total	21	14	72	13	108	24	58	15	57	23	47	19	11	7	2	5	1	0	497
Blacks:																			
I & II	0	0	2	0	10	8	1	1	5	0	0	1	0	0					28
III	0	0	3	0	6	5	2	1	0	0	0	0	0	0					17
IV & V	4	4	77	9	101	6	36	3	12	1	0	4	0	1					258
Total	4	4	82	9	117	19	39	5	17	1	0	5	0	1					303

* Hollingshead Social Class Index (ref. 4).

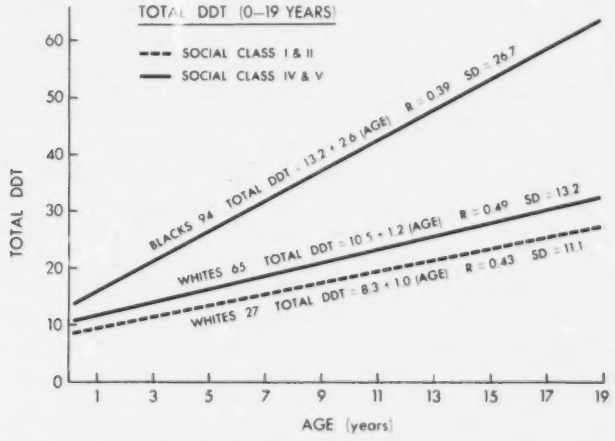

FIGURE 1. Regression of serum total DDT levels (ppb) on age in three general population subgroups of Dade County, 1970–1971.

of DDT and its metabolites but not dieldrin were age dependent (1, 6, 7). Man has been incidentally exposed to DDT for periods of time which have varied between 20 and 25 years, depending upon when this pesticide was first widely used. Age association, therefore, might be expected to reflect differences in years of exposure in the first two decades of life, but not among those 20 years of age and older. This study included residue data from 219 persons who were under 20 years old. The linear dependence of serum DDT, DDE and total DDT levels on age was studied in the younger age bracket as well as in the 20–89-year age group. Figures 1 and 2 show the association of serum total DDT residues with age in seven subpopulation groups in Dade County. Figure 1 illustrates age dependency of serum residues of total DDT derived materials within the first two decades of life and figure 2 illustrates age differences

in the older age groups. In the three groups for which sufficient data are available for the younger ages, the regression of this pesticide residue on age is much stronger among persons in the first two decades of life than it is in the 20 years and over age group. Principally because of this age association, further study of the relation of human pesticide residues with socioeconomic variables was restricted to persons 20 years and over. In three of the adult groups, the standard deviation about the line is large, only a small fraction of the group variability is accounted for by the regression equation. The single exception in the older groups is the strong relation of serum total DDT residues on age among 26 blacks, Classes I and II.

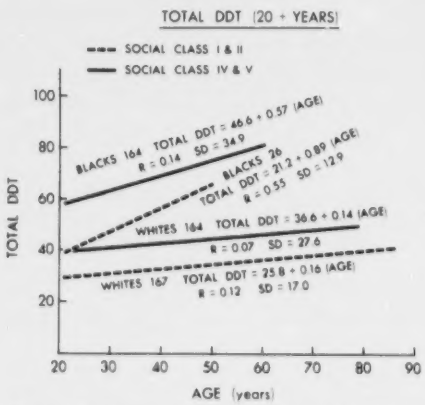

FIGURE 2. Regression of serum total DDT levels (ppb) on age in four general population subgroups of Dade County, 1970–1971.

It is apparent that the Hollingshead socioeconomic classification does not wholly account for the present differences in residue levels between races. However, this classification is effective in dividing each race into groups with different mean levels. It is worth noting that the differences between the races are greatest for the older age groups; the differences between the white social classes are fairly uniform for all ages 20 and over; the differences between the black socioeconomic groups are greater for the younger adults.

Table 2 presents individual regression equations of DDT and DDE in the three population subgroups under 20 years old and the four population subgroups 20 years and over.

With regard to sex differences, previous surveys had differed as to whether organochlorine residues were sex dependent (1, 2, 6, 7). Table 3 compares serum DDT, DDE

TABLE 2

Regression equation of serum DDT and DDE in general population subgroups from 0–19 years and 20 years and over, Dade County, 1970–1971

Age (years)	Social Class*	No.	Regression equation	r value	S.D.
0–19	I & II (Whites)	27	DDE = 6.9 + 0.67 × age	0.39	8.5
			DDT = 0.6 + 0.25 × age	0.52	2.1
0–19	IV & V (Whites)	65	DDE = 7.0 + 0.97 × age	0.53	9.9
			DDT = 2.7 + 0.08 × age	0.17	3.0
0–19	IV & V (Blacks)	94	DDE = 8.5 + 2.1 × age	0.40	20.4
			DDT = 3.7 + 0.33 × age	0.26	5.4
20–89	I & II (Whites)	167	DDE = 20.6 + 0.09 × age	0.09	13.2
			DDT = 2.8 + 0.06 × age	0.22	3.3
20–79	IV & V (Whites)	164	DDE = 28.1 + 0.08 × age	0.06	20.6
			DDT = 5.4 + 0.05 × age	0.13	5.7
20–50	I & II (Blacks)	26	DDE = 13.9 + 0.73 × age	0.56	10.3
			DDT = 5.7 + 0.08 × age	0.23	3.1
20–60	IV & V (Blacks)	164	DDE = 38.4 + 0.30 × age	0.09	27.1
			DDT = 3.7 + 0.24 × age	0.29	6.6

* Hollingshead Social Class Index.

TABLE 3

Comparisons of serum organochlorine residues in males and females (20 years and over) by race and social class, Dade County, 1970–1971

Race and sex comparisons*	Social Class	No.	Mean DDT†	Mean DDE†	Mean dieldrin†
White males	I & II	109	5.5	25.3	1.3
vs.					
White females	I & II	58	4.3	22.5	0.6
White males	IV & V	143	7.3	32.2	1.8
vs.					
White females	IV & V	21	7.9	24.9	1.6
Black males	I & II	16	7.9	37.6	1.3
vs.					
Black females	I & II	10	8.0	31.7	0.6
Black males	IV & V	149	10.0	47.2	1.1
vs.					
Black females	IV & V	15	14.2	42.9	1.6

* Two-sample *t* test.

† No significant difference at .05 level for each race and sex comparison.

TABLE 4

Serum levels of DDT (ppb) in 377 adult whites and 204 adult blacks, 20 years and over, by Hollingshead socioeconomic class, Dade County, 1970–1971

Race	Social Class	No.	Mean	Median	S.D.	Ranges
White	I	63	5.0	5	2.7	<2–11
	II	104	5.2	4	3.8	<2–23
	III	46	5.9	5	4.3	<2–21
	IV	126	7.2	6	5.6	<2–44
	V	38	7.9	6	6.0	<2–27
Black	I	12	7.7	8	2.6	3–13
	II	14	8.2	8	3.5	4–17
	III	14	7.9	8	3.2	3–13
	IV	89	9.7	8	6.7	3–53
	V	75	11.3	10	7.0	<2–35

and dieldrin residues in adult males and females stratified by race and social class. No significant differences were noted between males and females for each of these chemicals.

Tables 4, 5 and 6 present the mean, median, standard deviation and ranges of serum DDT, DDE and dieldrin, respectively, collected from 377 adult whites and 204 adult blacks 20 years of age and over, stratified by social class. The average levels for DDT and DDE increased in those social classes reflective of poverty in the whites; the same trend was suggested for the blacks, although the numbers in the upper and more affluent classes were relatively small. Similarly for dieldrin, average levels were greater in the whites, Classes IV and V, but this was not the case for this pesticide in the blacks.

It was felt that Social Class III reflected socioeconomic factors of both upper and lower social classes, so that statistical comparisons of serum pesticide prevalences were made for the combined Social Classes I and II with those of Social Classes IV and V (table 7). Mean serum levels of DDT, DDE and dieldrin were significantly

TABLE 5

Serum levels of DDE (ppb) in 377 adult whites and 204 adult blacks, 20 years and over, by Hollingshead socioeconomic class, Dade County, 1970–1971

Race	Social Class	No.	Mean	Median	S.D.	Ranges
White	I	63	22.3	20	10.4	8–50
	II	104	25.6	21	14.6	1–78
	III	46	29.9	25	26.7	5–187
	IV	126	30.4	26	19.0	3–163
	V	38	33.9	28	25.2	5–132
Black	I	12	33.1	30	11.3	18–50
	II	14	37.2	37	13.0	18–67
	III	14	29.1	27	10.0	14–49
	IV	89	43.8	38	24.1	16–159
	V	75	50.5	44	30.1	4–180

TABLE 6

Serum levels of dieldrin (ppb) in 377 adult whites and 204 adult blacks, 20 years and over, by Hollingshead socioeconomic class, Dade County, 1970–1971

Race	Social Class	No.	Mean	Median	S.D.	Ranges
White	I	63	1.1	1	1.2	<1–5
	II	104	1.0	1	1.2	<1–5
	III	46	0.9	1	1.1	<1–4
	IV	126	1.7	2	1.6	<1–11
	V	38	2.1	2	2.3	<1–9
Black	I	12	1.1	1	1.2	<1–3
	II	14	1.0	1	1.5	<1–4
	III	14	0.4	1	0.6	<1–2
	IV	89	1.1	1	1.1	<1–4
	V	75	1.2	1	1.3	<1–5

TABLE 7

Comparisons of serum pesticide residues (ppb) by social class (Hollingshead) of 331 adult whites and 190 blacks (20 years and over), Dade County, 1970–1971

Race	Comparison groups	No.	Mean DDT	Mean DDE	Mean dieldrin
White	Social Classes I & II	167	5.1	24.3	1.0
	vs.				
	Social Classes IV & V	164	7.4	31.2	1.8
	t test*		$p < .001$	$p < .001$	$p < .001$
	F test†		$p < .05$	$p < .05$	$p < .05$
Black	Social Classes I & II	26	8.0	35.3	1.0
	vs.				
	Social Classes IV & V	164	10.4	46.8	1.1
	t test*		$p < .01$	$p < .001$	NSD‡
	F test†		$p < .05$	$p < .05$	NSD‡

* Two-sample *t* test.
† Significance of homogeneity of variance.
‡ No significant difference at .05 level.

greater in the poorer classes (IV and V) than in the white more affluent classes (I and II) ($p < .001$, $p < .01$, $p < .001$, respectively). The same significant differences in blacks were noted for DDT ($p < .01$) and DDE ($p < .001$) but not for dieldrin (no significant difference). In both races there were no significant age differences between Social Classes I and II, and IV and V.

Not only were the means significantly greater in the poorer classes but the variances also, as measured by the *F* test, were different in these social class comparisons except for dieldrin in blacks. Within the classes blacks still had greater residues of DDT and DDE.

In addition to the Hollingshead Two Factor Index, the census tract median income and population density (1960 data; 1970 data not available) were used as yardsticks of the social class of the community (table 8); here again, residues were found to be higher in the less affluent areas (figure 3).

Irrespective of the stratification used, the same trend was observed, indicating greater concentrations of the metabolite with poverty and overcrowding. The census tract median income data were also used to measure the representativeness of the study group by comparison with the distribution of this parameter for the whole county; with few exceptions, the profile of the study group was representative of the socioeconomic profile of the total community.

TABLE 8

Percentage distribution by census tract (1960) of median income of Dade County and distribution in study sample*

Rate	Income	% census tract	% study group
White males	$6,000+	29.2	32.4
	$5,000–$5,999	14.4	24.6
	$4,000–$4,999	21.0	16.5
	$3,000–$3,999	14.4	19.7
	<$3,000	9.4	6.7
Black males	$6,000+	1.7	4.6
	$5,000–$5,999	2.1	4.6
	$4,000–$4,999	2.5	22.0
	$3,000–$3,999	40.5	40.5
	<$3,000	53.3	28.3

* 1970 data not available.

DISCUSSION

The objective of this study was to ascertain whether higher levels of DDT and its metabolites noted in blacks in the earlier

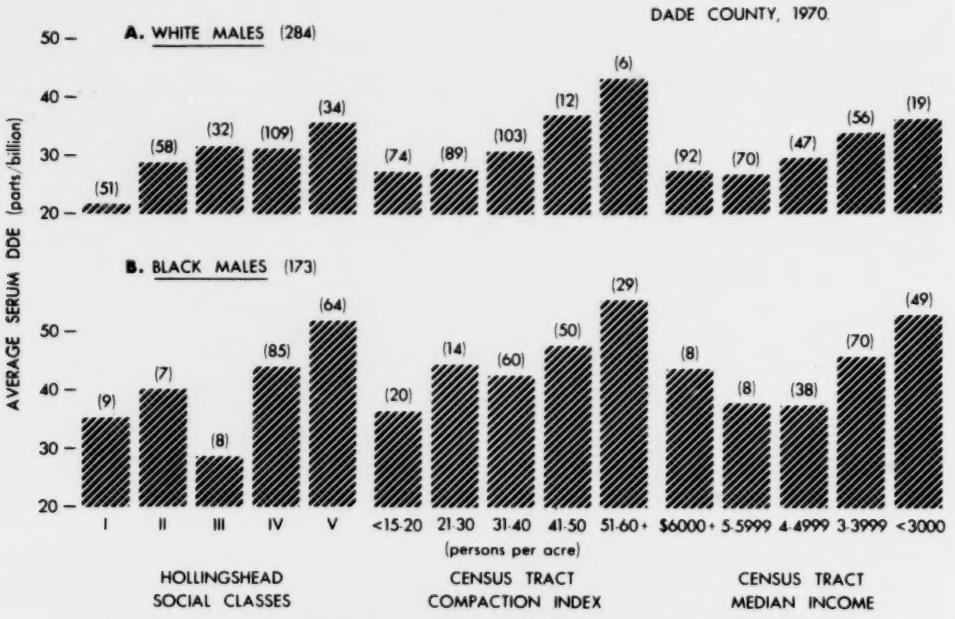

FIGURE 3. Average serum DDE residues (ppb) in general population (males only) by Hollingshead Index, compaction index (population density) and median income.

U.S. population surveys were associated with factors related to social class. Before these could be measured, it was necessary to determine if age and sex were significant variables of incidental exposure in this area. DDT and DDE traces were strongly correlated with age in the first two decades of life but negligible in the older age groups. Dieldrin concentrations were too small to permit an age appraisal. There was no significant association with sex for any of the pesticides so that the total adult population, 20 years and over, was used to study the effects of socioeconomic variables. The data supported the concept that much if not all of the race-associated differences in DDT levels could be explained on the basis of factors associated with social class. Dieldrin residues, which were greater in the less affluent whites but not in the blacks, probably reflected different domestic pesticide use patterns. Since residues of DDE were also found to be positively associated with increasing poverty and overcrowding in the city, one might speculate that such variables as housing, the adequacy of garbage disposal, the presence or absence of fly screening, and differences in individual domestic pest control practices were some of the more important factors of social class which contributed to these differences. There are both epidemiologic and public health consequences of this association.

Epidemiologically, the human pesticide residue has been used to express national prevalences of incidental exposure, to make international comparisons, to compare secular trends of incidental human pollution and to compare prevalences in health and disease. The demographic distribution characteristics of the human DDT residue make evident the future need for sample representativeness if expressions of national prevalences are being sought. The demonstration of a significant and predominant age correlation of serum levels of DDT and especially DDE levels, calls for a reappraisal of earlier interpretations of secular trends of

incidental DDT exposure, at least in this area where domestic exposure is considerable. Theoretically, there are at least three possible explanations for these age trends. The first is that the trend is a cohort effect and the DDT exposure in the present 0–10-year age group is less than it was 10 years ago for the cohort which is now in the 10–20-year age group. The second possibility is that this is a host characteristic and one which is in some way or other related to growth and adolescence. The third possibility is that because DDT has been widely used for about 20 years, the greater age correlation of DDT residues in this period of life is really a reflection of the DDT age of our society and that if use patterns were to continue, subsequent age groups would continue to show the increase with the duration of DDT exposure. Whichever of these explanations is correct, the trend emphasizes the need for ongoing human monitoring studies if we wish to measure the incidental exposure on a global basis.

Epidemiologic investigations into the health effects of pesticides usually employ one or two analytical techniques. Comparison of morbidity rates in the occupationally exposed with controls has been one approach and comparison of tissue residues in disease with levels in healthy controls has been another. So striking is the association of DDT residues with social class, that one might predict higher residues in diseases associated with poverty. Such an association would be indirect rather than causal, and studies which failed to match for this variable might provide data which could be readily misinterpreted.

From a public health point of view, the socioeconomic association of the human DDT residue again questions whether food is the major source of this residue in all parts of the world. While food may be the major source in the cooler parts of the world, the DDT prevalence data here reflect the special social and environmental characteristics of a favorable climate which produces an increased pest problem. The control of flies, mosquitoes and cockroaches is essential for human comfort and the increased domestic use of insecticides becomes a significant nondietary source. If we follow this concept to its ultimate conclusion, then it will be necessary to monitor man as well as his food, if we wish to measure this incidental exposure on a global basis.

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8. SAFETY PROBLEMS RELATED TO EXPOSURE OF WORKERS IN PESTICIDE FORMULATION PLANTS

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Workers in pesticide formulation plants are often exposed to relatively high levels of pesticide compounds. Since most chemical pesticides have at least some degree of toxicity to man, it is important that all workers, as well as management, be aware of any potential hazard that may accompany exposure to such compounds. Experience has shown that if proper precautionary measures are observed, workers can safely handle even the more toxic compounds. Although pesticides cause illnesses and even deaths each year, many of these cases are a result of carelessness or accident. Proper education as well as close supervision of workers may prevent some accidents and greatly reduce the number of illnesses resulting from carelessness.

The main purpose of this chapter is to discuss some of the problems related to exposure of workers in formulation plants, to indicate various ways that unnecessary exposure to pesticides may occur and to point out certain precautions to prevent such exposure. Discussions of medical supervision, clinical aspects of poisoning, antidotes, the effect of pesticides on the body and steps to take in case of poisoning are given in chapter 10.

EDUCATION OF EMPLOYEES

It is essential that all employees, regardless of their duties, have at least some knowledge of pesticides. Well-informed personnel are more likely to take proper precautionary measures when handling toxic materials and thus help to maintain a good safety record for the formulation plant. The personnel should be informed about the different classes of pesticides, i. e. chlorinated hydrocarbon, organophosphate, carbamate etc., and their relative toxicity. Pesticide workers should be aware that pesticides may enter the body by more than one route, and that these routes of entry must be protected in order to avoid excessive absorption of pesticides. One or more persons should be trained in first aid and be competent in the proper application of artificial respiration. The consulting physician may advise that workers be given enough information about some of the more characteristic signs of poisoning so that they will recognize them and report to the supervisor.

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Medical supervision

Regardless of the size of the plant operation, it is wise to arrange some type of medical supervision. This is particularly important if highly toxic chemicals are being formulated. Regular employees should be given a physical examination at least once a year. A pre-employment physical examination should include a blood cholinesterase test for employees who may work with the more toxic cholinesterase-inhibiting compounds. This test will provide some indication of the normal cholinesterase activity level and may be useful later in determining whether an illness is due to pesticide poisoning. Personnel working with such compounds, especially the highly toxic organophosphate pesticides, should have their cholinesterase activity checked at regular intervals in order to detect any appreciable deviation from normal which may indicate impending danger of poisoning. If significant reduction in cholinesterase activity is noted, the employee should be removed from the work situation, which might be a source of exposure to pesticides, until the worker is advised by a physician that it is safe to resume his regular duties.

Selection of workers

Risk of injury or illness should be minimized by using the best informed and most careful employees in work situations that are potentially the most hazardous. Unfortunately, this principle is not always observed. The more hazardous jobs are usually dirtier, require more physical effort and thus are less desirable than other positions in a formulation plant. As a consequence, new, inexperienced personnel are often given the more hazardous jobs, while those with more seniority and knowledge of pesticide safety move to the more desirable positions.

Careless workers are not particularly difficult to detect. Some fairly close observations of their work activities quickly reveal this tendency. For example, careless operation of equipment such as the bagging machine may soon cause an excess of dry pesticide formulation in the air and around the formulating machinery even though relatively efficient ventilation equipment is in operation. Such excess dust in the air may settle to form a layer of contamination on clothing, equipment, warehouse structural components and flooring.

Employees should not be allowed to work alone when handling hazardous pesticides. In some plants a "buddy system" is practised whereby each worker is assigned a partner who is required to know at all times where the other worker is located in the work area.

Plant ventilation and safe use of equipment

In the formulation plant, it is important that the ventilating system be maintained under negative atmospheric pressure so that any leakage will result in inflow of air, thus reducing the contamination of the work environment.

Where there is lack of adequate supervision, workers often neglect to report malfunctioning ventilation equipment; they may fail to use exhaust fans, and they sometimes open doors that allow gusty winds from outside the building to blow contamination throughout the plant.

Considerable care must be exercised when operating equipment for moving large drums of liquid emulsifiable concentrate pesticides. When a single worker tries to handle the drums, he runs a greater risk of dropping the drum or spilling the concentrate. Therefore, to avoid accidents, two persons should be assigned the job of moving heavy drums of pesticides.

In mixing liquid formulations, the use of a closed system reduces the workers' chance of exposure. During filling of containers, however, there is some chance of exposure if protective gear is not worn.

Filler spouts and nozzle mechanisms for dry pesticide packaging must be kept in good working condition to prevent excess exposure of the worker. If the auger or other feeder mechanism in the filler spout assembly malfunctions, there is a large risk of a heavy exhaust of dry pesticide at a time when the bag may not be in place. In one recorded case, the filler mechanism of a 50-lb size bagging machine nozzle was accidentally pushed, so that 1 per cent TEPP dust was blown out with considerable force. The workers near the bagging station were engulfed with the highly toxic material, and about 50 lb of the material accumulated on the floor around the bagging station. Fortunately, the workers were wearing goggles, tight-fitting respirators and other protective clothing. The machine had malfunctioned several times prior to the incident but no effort had been made to correct the situation until the more serious incident occurred.

Containers can be punctured because of careless operation of fork-lift trucks used in formulation plants to move pallets loaded with bags or cartons of pesticide. The relatively sharp ends of the fork can easily tear a bag or rupture a drum. This may result in leakage during storage and transportation. Contents of dented drums or punctured bags should be placed in new undamaged containers before shipment from the formulation plant.

GOOD HOUSEKEEPING

Good housekeeping is essential if environmental exposures are to be kept at a minimum. All spillages should be cleaned up at once. Liquid spillages should be picked up with absorbent material. In the plant, some form of dry inert material should be kept on hand for this purpose. Fine sawdust, attaclay or other fine inert absorbent material are effective.

Large quantities of dry pesticides can be picked up with a broom and dustpan. Sweepings should be placed in a special container labelled as "waste pesticidal material". A product-labelled container should never be used as a waste pesticide container. Lighter accumulations of dry pesticides on floors or other surfaces can be picked up with an industrial vacuum cleaner. An extremely smooth concrete floor is much easier to clean than one that has not been carefully finished or one that is made of wood. Thus, during construction of a formulation plant it is

advisable to expend the extra effort needed to produce a very smooth floor finish. Smooth floor surfaces can be kept clean by using chemically treated dust mops with a sweeping compound.

Protective clothing and devices

Protective clothing and devices should be worn and used during all work with pesticides in order to protect the routes of entry into the body. The four routes of entry are dermal, respiratory, oral and direct entry into the blood stream through cuts or abrasions.

The dermal route is probably the one that is often overlooked by workers. Most persons are aware of the danger of inhaling or swallowing insecticides but the possibility of absorbing appreciable amounts of poison through intact skin is not as familiar. Yet this route has probably been responsible for a great many poisonings, especially from the organophosphate compounds. Dermal exposure is particulary important where liquid concentrate compounds are involved. The main body area can best be protected dermally by the use of water-repellent clothing; however, in most formulation plants the usual attire is cotton coveralls and a waterproof apron. The waterproof apron is especially needed by the worker at the bagging or mixing stations, as there is often considerable contamination on the front of his clothing. Even when the waterproof apron is used, it is very important that the worker change to freshly laundered clothing each day. A common fault in many plants is inadequate protective gear for the head. Head coverings or caps are often made of material that is easily penetrated by toxic pesticide. Certain heavy exposure situations may require goggles or a face shield to protect the eyes and face. Rubberized boots are essential in formulation plants. The legs of coveralls should be worn outside the boot tops to prevent dry pesticide from sifting into the footwear.

Hands should be protected by use of unlined gauntlet-type natural rubber gloves. The gauntlets protect the wrist area not normally covered by the sleeves and, since they have no cloth lining, they are also easier to clean on the inside. Heavyweight gloves, although durable, do not allow adequate freedom of movement or finger flexibility; furthermore, they are difficult to turn inside-out for proper cleaning. On the other hand, some lightweight gloves, although flexible enough to allow freedom of finger movement, wear out rapidly and are easily torn. Therefore, it is advisable to secure gloves of a durable quality but light enough to be easily turned inside-out for daily cleaning.

The respiratory route of exposure should be protected by a respirator capable of filtering out the compound in question. The filter cartridges should be changed after 8 hours of appreciable exposure and more often if pesticide odour is detected through the mask. If the filter pads are separate, removable items, they should be changed twice a day or more often if filter clogging causes difficulty in breathing. Gas masks with canister-type filters should be used when high concentrations of highly toxic vapours are present or when the worker is subjected to prolonged exposure in confined spaces. Use of a self-contained air supply respira-

tor is advisable when working inside blender tanks or dust hoppers during cleaning or repair operations.

To be effective, the respirator should fit tightly enough against the face to prevent leakage. After a period of use, the cartridges and filters should be removed and the facepiece washed with soap and water. After drying, the cartridges and filters should be replaced and the proper position of the seals or gaskets should be checked. The respirator should be stored in a container in a dry place. A respirator should never be hung by the straps over a nail on a wall for storage. If it is hung by the headbands they may stretch and lose elasticity, so that it is difficult to get an airtight seal with the face the next time the respirator is worn.[1]

Personal hygiene

Even though the employer may provide a relatively safe working environment, the formulation plant worker should make an effort to protect himself from excess absorption of pesticides through good personal hygiene practices. Upon arrival at work, the worker should remove his street clothing and put on clean work clothing. No street clothing should be worn under work clothing. At the end of his work shift he should remove the clothing and place them in a bin to be laundered. He should then bathe in a shower using plenty of soap to thoroughly cleanse any pesticide from the skin before dressing in his street clothing to go home. If a worker should become excessively contaminated at any time with either a dry or liquid concentrate pesticide, he should immediately stop work, bathe and change into clean work clothing before resuming his duties. This is especially important if he has been working with the more toxic organophosphate compounds. In such a case the worker should be observed for poisoning symptoms. In most plants, the employer furnishes freshly laundered protective clothing daily.

The worker should be responsible for daily cleaning of waterproof protective clothing such as aprons, boots and gloves. It is especially important that rubber gloves be thoroughly cleaned on the inside as well as the outside. He should inspect his gloves regularly for small holes or tears and destroy those that are found to be defective.

Workers should never smoke, chew tobacco or gum, drink or eat while working with pesticides. These activities should take place away from the pesticide formulation area preferably in a separate room provided for that purpose. The hands and face should be washed before eating, drinking or smoking.

Measurement of exposure

If there is any question about the degree of exposure in different work situations in the formulation plant, both indirect and direct methods of measure-

[1] Protective clothing when worn in hot climates may prove extremely uncomfortable to the workers, and special incentive pay may be necessary to maintain strict adherence to personnel protection regulations.

ment are available. An example of an indirect method of measurement that correlates quite well with the clinical effect is the determination of cholinesterase activity in the blood of workers exposed to organophosphate compounds. Determination of urinary metabolites excreted following exposure is another example of indirect measurement of exposure. The level of excretion of p-nitrophenol in the urine of persons exposed to parathion and the level of dichlorodiphenylacetic acid in the urine following exposure to DDT have been useful tools to determine the level of exposure in a particular work situation.

Because many pesticides are not cholinesterase-depleting compounds and because urinary metabolites for many compounds are not known, direct methods may be needed for measuring potential exposure. Potential dermal contamination can be measured by swabbing skin areas or by attaching special absorbent pads to different parts of the body or clothing of workers. Contamination of the hands can be measured by rinsing them with a suitable solvent into a polyethylene bag. The amount of pesticide found on the dermal pads, swabs or bag rinses will indicate the amount of pesticides that may have accumulated on exposed skin areas during a specific period of work activity. Respiratory exposure can be estimated from the contamination of filter pads held in special single- or double-unit respirators, from air concentration values determined by use of impinger-type air samplers or both. Chemical analysis of respirator pads or of air samples taken near the breathing zone of workers yields values that can be used to calculate the potential respiratory exposure.

Disposal of waste pesticides and empty containers

A problem that can be a serious hazard to the public is the improper disposal of waste pesticides that have accumulated in formulation plants from spillages, floor sweepings etc. Pesticides should never be washed into a drain or flushed into a sewage system. The best method of disposal is burial under at least 18 inches (45 cm) of soil in a location carefully selected to ensure that no surface or subsurface water will become contaminated. Adding lime or lye (sodium hydroxide) is sometimes recommended to hasten the degradation of certain compounds. However, this method is not completely reliable to make the buried material completely non-toxic. Neutralizing the poisonous effects of most pesticides is not easy, especially where large quantities of the toxic material are involved. Burning large quantities of pesticide wastes is not advisable because of possible air pollution. Even use of especially built incinerators where very high temperatures produce relatively complete combustion does not assure that no toxic smoke or vapour will be emitted.

The disposal of empty pesticide containers should not create a hazard for humans or animals. Combustible containers, such as paper bags and cartons, can be destroyed by burning; however, in some areas there is an objection to this practice because of the creation of air pollution. If such containers are burned, extreme caution should be used, and smoke should be avoided. In the United States, formulation plants usually have incinerators for burning combustible

containers. Such incinerators should be enclosed by a high fence with a padlocked gate to keep out unauthorized persons. If combustible containers are not burned they should be buried.

Disposal of metal drums presents a greater problem. The drums should be returned to the manufacturing plant, but if this is not possible they should be thoroughly drained and rinsed with a decontamination solution. The National Agricultural Chemical Association of the United States has published the following procedure for rinsing different size drums which had contained organophosphate pesticides:

> For the 5-gal size, use 2 quarts of water, 2 tablespoons of detergent and $\frac{1}{3}$ cup of lye. For the 15-gal size, use 1.5 gal of water, $\frac{1}{4}$ cup of detergent and $\frac{1}{2}$ lb of lye. For the 30-gal drum, use 3 gal of water, $\frac{1}{2}$ cup of detergent and 1 lb of lye. For the 55-gal drum, use 5 gal of water, 1 cup of detergent and 2 lb of lye.
>
> Carefully add the rinse solution to the drum and then rotate the container to completely wet all inner surfaces. Let the container stand at least 15 minutes with occasional agitation. Remove all bungs or stoppers and drain the rinse into an area where there is no chance of runoff into water supplies. Next, thoroughly flush both the inside and outside of the container with clean water.

Although the procedure may not completely detoxify or remove absolutely all pesticide from drums, it should render them much safer than if no rinse were used.

After the decontamination rinse, the bottoms of the drums should be punctured and the drums should be buried in a safe location as described above for combustible containers. Drums should not be allowed to accumulate in an area accessible to unauthorized persons who may be tempted to use them for trash-burning containers, livestock water troughs, storage cans or other purposes.

Decontamination of containers which have held other types of pesticides, including chlorinated hydrocarbon and carbamate compounds, requires more rigorous treatment than that described above. The manufacturing plant should be consulted for specific procedure to decontaminate drums that contained such compounds.

Summary

Workers in pesticide formulation and production plants are often exposed to relatively high levels of pesticide compounds; therefore, it is important that all workers, as well as management, be aware of any potential hazard that may accompany exposure to such compounds. Personnel should know the precautionary measures that must be taken when working with different compounds, the routes of entry of pesticides into the body and how to protect these routes. Regardless of the size of the plant operation, some type of medical supervision of employees is desirable. Risk of injury or illness can be minimized by using the best informed and careful employees in work situations that are potentially

the most hazardous. Care should be used in operation of equipment in order to avoid unnecessary contamination of the working environment. Protective clothing and devices should be used and be properly maintained. Good personal hygiene practices should be encouraged in order to reduce absorption of pesticides. Both direct and indirect methods of measurement of exposure in different work situations are available for certain compounds. Care should be employed in disposing of waste pesticides and empty containers.

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HEALTH HAZARDS IN THE AGRICULTURAL USE OF ECONOMIC POISONS[1]

PUBLICATION

82

TOXICOLOGY PROGRAM
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The development and use of new pesticides during recent years has been a great boon to agriculture through the production of more and better food for the growing population. We must bear in mind, however, that there are hazards that accompany the use of such materials, particularly when they are misused. Each year there are illnesses and deaths that are attributed to pesticides, especially the more toxic organic phosphorus compounds. These deaths are usually the result of gross carelessness or accident. A realization of the hazards inherent in pesticide materials, however, should not discourage their use but rather should stimulate safer handling of them.

The U. S. Public Health Service has been attempting to encourage safer handling of such materials and has conducted studies to evaluate the potential health hazards associated with the intensive use of various economic poisons. Studies at the Wenatchee Field Station have been concerned mainly with three general segments of the population: (1) workers who have more direct contact with toxic pesticides, such as the formulator, the spray or dust machine operator, or other workers exposed to residues on crops; (2) persons not directly or intentionally associated with the chemicals, including those persons exposed when spray or dust drifts into dwellings during application to adjacent fields or orchards, and children or irresponsible adults who come in contact with so-called "empty" pesticide containers or those who accidentally drink from a beverage bottle or other unlabeled containers that have been carelessly used for storage of small quantities of liquid pesticide; and (3) the general population, all of whom are exposed to residues in food.

Hazard to Persons Who, Through Their Work, Have Direct Contact with Pesticides

Workers in plants formulating agricultural pesticides are often exposed to large amounts of toxic chemicals. However, they are the group that is usually most aware of the potential danger of exposure and are usually provided with and use protective equipment such as respirators and clean coveralls. Also, they are more inclined to bathe immediately following a period of exposure. Even with these precautions, there have been cases of pesticide poisoning in this group, especially where organic phosphorus insecticides have been involved.

Also, the individual who applies certain pesticides by spray or dust machine also may have a heavy potential exposure. He should be aware of the danger involved and has a chance to protect himself if he chooses. Studies have been conducted to determine the potential exposure to spraymen applying various pesticides. This type of measurement involved the assay of dermal

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exposure by attaching absorbent patches on the skin of workers during actual spray operations. Respiratory exposure was measured by analyzing the filter pads from each worker's respirator and by determining, through air sampling, the amount of toxicant in the air near the breathing zone of the operator. Batchelor and Walker (1954), measuring potential exposure to parathion in orchard areas of central Washington, reported that contamination by the dermal route was greater than that by the respiratory route.

Durham and Wolfe (in preparation) estimated that an average orchard sprayman who wore no hat or no protective clothing on his arms would potentially be subjected during each hour of spray operations to about 7.7 per cent of the toxic dose of parathion as calculated by extrapolation from data on toxicity studies in laboratory animals. According to this data, one might calculate that after approximately 13 hours of spraying an individual could become poisoned. Use experience has shown that this is not necessarily true, however. The relative innocuousness of this large skin contamination may be explained by slow and/or incomplete absorption of the pesticide which impinges on the skin. In this connection, Rothe et al. (in preparation) have shown that rats can withstand more than an LD_{50} (the dosage required to produce a 50 per cent mortality in experimental animals) of parathion daily for many days without significant injury, provided the material is given in their food so that the dose is received gradually rather than instantaneously, as in the case of a single, acute dose given by stomach tube. In other words, a part of the reason that poisoning is no more frequent is that the dosage absorbed from the skin is distributed over many hours. The hazard to spraymen is also alleviated considerably by the fact that most of them wear a hat that affords some protection from drift onto the face and neck area and they also often wear long sleeves for protection of their arms.

Durham and Wolfe also measured exposure to one of the most widely used insecticides, DDT. They estimated the potential exposure to be only 0.15 per cent of the toxic dosage per hour of spraying with an air-blast machine in orchard areas. Batchelor et al. (1956) calculated the potential exposure of orchard spraymen to dinitroorthocresol during its use as a blossom-thinning spray for apples to be about 0.25 per cent of the toxic dose per hour of spraying.

Although the largest portion of our research concerns insecticides, illnesses allegedly due to fungicides and herbicides are also being studied. All available case reports of accidental ingestion of these compounds are being collected.

In the field of herbicides, Wolfe et al. (in preparation) measured the exposure to operators of ground spray machines when applying dinitro-o-secondary butyl phenol (commonly referred to as DNOSBP or dinitro amine) as a weed control spray in fields of peas and corn in western Washington. The potential exposure was calculated to be 0.96 per cent of the toxic dose during each hour of spraying. In Europe, there have been a number of illnesses and some deaths among ground spray machine operators applying dinitro compounds for weed control. However, results of the above study of exposure and levels of the compound found in the urine of the spraymen involved indicate that no significant hazard is associated with the application of DNOSBP for weed control under conditions of its use in western Washington, providing it is applied in the recommended manner. This conclusion has been corroborated by use experience.

One of the most widely used herbicides is 2, 4-D. This compound is not very toxic to experimental animals. Its oral LD_{50} to white rats is about 500 mg./kg. as compared to 125 mg./kg. for DDT. Use experience with 2, 4-D has generally been good from the standpoint of human health. There is a single report (Goldstein et al., 1959) of three cases of peripheral neuropathy in persons who had a history of exposure to 2, 4-D. These three cases were all seen in a single hospital during a three month period.

In cases of extensive respiratory exposure or accidental ingestion of commercial formulations of 2, 4-D herbicides, the aliphatic or aromatic solvents used may cause certain poisoning symptoms characteristic of the solvents but not of 2, 4-D.

Another facet of the exposure of workers to pesticides involves residue on crops. The ability of parathion residues on foliage to poison crop workers has not been generally appreciated. Quinby and Lemon (1958) reported eleven instances of parathion residue poisoning in crop workers. Etiology was confirmed by a lowered blood cholinesterase level and by improvement following atropine. Of a total of 142 persons exposed, 75 became ill. These mild poisonings occurred in workers thinning, picking, or irrigating crops of apples, pears, grapes, oranges, and hops treated with one or more pounds of parathion per acre. Several of the known instances of poisoning involved exposure to foliage or fruit sprayed not more than two days earlier. However, contact with pear trees, grape vines, and orange trees caused poisoning as much as 12, 33, and 34 days, respectively, after application. Since the reporting of this clinical and occupational type of parathion poisoning, there have been found many more such outbreaks involving hundreds of workers.

Hazard to Persons Not Directly or Intentionally Associated with Pesticides, Including the General Population

Another segment of the population that has been considered in studies of exposure to pesticides is the group of persons not directly or intentionally associated with pesticide applications. The hazard to residents from spraying adjacent orchards has been evaluated by Summerford and co-workers (1953) in extensive studies carried out in 1951 and by Hayes and colleagues (1957) in studies done in 1952 and 1953. This work involved study of blood cholinestrase levels and incidence of illness among groups of persons with different degrees of exposure to organic phosphorus insecticides.

Blood cholinesterase values were found to be depressed during the period of exposure for those groups of workers, including formulators and spraymen, having definite exposure. No change in blood cholinesterase during the spray season was seen in the groups of individuals (including residents in or near orchards) with little or no exposure. Illness suggestive of poisoning was increased in the definitely exposed groups during the period of their exposure. Illness resembling mild poisoning was not significantly more common in persons (including those residing in or adjacent to orchards) living in an agricultural community who had no occupational or gross accidental exposure than it was in persons living in a non-agricultural area, where insecticides were not used.

A recent advance in analytical chemistry has given us a new tool in this area of study. Elliott et al., (1960) developed a more sensitive procedure for the measurement of exposure to parathion. This procedure involves the assay of urinary excretion of p-nitrophenol, which is a parathion metabolite. This technique has been found to give a more sensitive measurement of exposure to parathion than does blood cholinesterase activity. By using this method, it was found that workers with higher degrees of parathion exposure generally excreted easily measurable quantities of p-nitrophenol, even though many showed no effect of the exposure on their blood cholinesterase activity. On the other hand, the average p-nitrophenol excretion of the orchard residents group was insignificant. This more sensitive measure of exposure essentially confirms earlier results with blood cholinesterase tests and symptomatology that the incidental exposure to residents in or near orchards during spray operations generally is insignificant.

Another hazard that has been evident for many years results from the apparent laxity on the part of some farmers to properly dispose of certain types of toxic pesticide containers after they have been emptied. As a result of this carelessness, children often become poisoning victims when playing with "empty" pesticide containers. Also, each year, tragic preventable poisonings occur when children drink from beverage bottles or other containers that have been filled with insecticide. Spray operators should make a special effort to dispose of empty pesticide containers so that children or irresponsible adults cannot come in contact with them.

The general population in this country is exposed to pesticide residues on food. There have been no cases of illness in this country from insecticide residues on food when formulations have been used according to directions (Hayes 1960). It is important, however, that long-term toxicity studies be continued to rule out the possible effects of chronic exposure.

Pesticide Poisoning

Each year, the U. S. Public Health Service Laboratory at Wenatchee, Washington, investigates a number of pesticide poisoning cases that occur in the Northwest. A higher incidence of poisoning occurs in some years than others. For example, during the 1958 spray season, there occurred a larger number of illnesses due to pesticides in central Washington. This included two fatalities and many illnesses, some very serious. Most of the poisoning cases involved parathion, the most widely used of the more toxic pesticides in that area. However, demeton (Systox) and Phosdrin were also involved.

Several factors may have been involved in this higher occurrence of poisoning observed during 1958. First, development of resistant strains of insects and mites brought about greater than normal usage of pesticides. Secondly, the 1958 spray season in central Washington was extremely hot. There are some indications that poisoning occurs more often in hotter weather. This may be because spraymen tend to wear less protective clothing in hot weather. Increased skin absorption and greater volatilization of the toxicants should also be considered. Thirdly, spraymen may have become a bit lax in observing safety precautions after experiencing several years of usage with no adverse effects.

These organic phosphorus pesticides poison by inactivating the enzyme cholinesterase, which results in an accumulation of excess acetyl choline, thereby producing symptoms of over-stimulation of the parasympathetic nervous system. Atropine, which acts only as an antagonist to the excess acetyl choline, has proved to be an effective antidote in cases of poisoning. In severe cases, artificial respiration may be lifesaving, since the usual cause of death is respiratory failure. More recently, a group of "true" antidotes for organic phosphorus poisoning has been found. The most widely used of these new antidotes is pyridine-2-aldoxime methiodide or 2-PAM. These compounds reactivate the enzyme which had been inhibited by the organic phosphorus compounds. A supply of 2-PAM is available at the laboratory in Wenatchee as well as at hospitals in several locations in the Northwest.

Summary

The U.S. Public Health Service has conducted studies to evaluate the potential hazard of pesticides to three segments of the population. The segment that includes the formulator, spray or dust machine operator, or other workers having closest contact with pesticides was found to have the greatest potential exposure. If they do not follow the recommended safety precautions when working with hazardous compounds, they may risk illness or death. The exposure to persons having only incidental environmental exposure as a result of spray or dust applications appears generally to be too small to constitute a significant health hazard. There have been no cases of illness in this country from insecticide residues on food when formulations have been used according to directions, but there have been when recommendations were ignored.

Each year tragic preventable poisonings occur when children come in contact with so-called "empty" pesticide containers or drink from beverage bottles or other containers that have been carelessly used for storage of small quantities of liquid pesticide.

Progress has been made toward finding a new antidote for organic phosphorus poisoning.

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PESTICIDE
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Significance of Pesticide Residues to Human Health

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Abstract

The use of chemical pesticides provides a number of health benefits, including control of insect-vector-borne diseases and increased food production. However, the use of these toxic materials on man or in his immediate environment has created potential hazards that are of great public health significance. Use experience data for pesticide manufacturing plant workers, formulators and spraymen under study by the Food and Drug Administration shows subtle biochemical differences related to high-level pesticide exposure. The significance of these differences is not known. The sensitivity of currently available chemical techniques has made possible the measurement of very small amounts of the chlorinated hydrocarbon pesticides in the environment and in human tissues, including blood. DDT levels in adipose tissue of the United States general population have not increased since they were first measured in 1950. However, current studies have shown that race, geographic location, and age are all important factors in determining the DDT storage level for an individual. Recent tests in experimental animals suggest that teratology from 2,4,5,-T formulations, potential carcinogenicity of DDT, and in-

duction of drug metabolizing enzymes by various chlorinated hydrocarbon pesticides are problems whose significance for human health must be evaluated. In two-year human volunteer studies, daily doses of DDT up to 200 times the ordinary dietary level did not produce detectable adverse effects. The single most important factor in determining toxicity, including cancer and teratogenicity, is dosage.

Introduction

The widespread occurrence in the environment of any foreign chemical is a matter of public health concern. The pesticides are poisons, of course, or they would not be useful in the control of insects, rodents, and other undesirable animals and plants. The possible harmful effect to the general population from intake of small amounts of these pesticidal chemicals as residues in food, water, air, or from other sources must be evaluated. In determining the overall effect on public health, the health benefits of pesticides must also be considered. Pesticides promote health directly through control of insect-vector-borne diseases and indirectly through increased and improved agricultural production of food and fiber.

Benefits of Pesticides

Disease control. Beginning with the introduction of DDT into vector control use during World War II, the effectiveness of these modern pesticides against a wide range of disease vectors has made possible the control of many important diseases which previously defied all practical efforts at control. Recent reports by the World Health Organization indicate that the control of many of the most important vectors of human disease is still almost entirely dependent on insecticides and no effective or economically feasible alternatives are available.

Control of malaria represents most dramatically the result of disease control by pesticides. Malaria has been generally considered to be the most important disease of man and has been stated to cause as many as 200 million illnesses and 2.5 million deaths per year.

Malaria was at one time an important disease in parts of the United States. For example, Barnes reported (2) 112 deaths and several thousand cases of malaria in California in 1910. Intensive control measures against the mosquito gradually reduced the disease, but it was not until DDT became available that malaria was virtually eradicated from this country. Statistics from many other countries are even more impressive. DDT has been the main agent in eradicating malaria in countries whose populations total 550 million people. This world-wide malaria control campaign carried out by the World Health Organization (16) has been estimated to have saved 5 million lives and prevented 100 million illnesses during its first 8 years and has recently reduced the annual malaria death-rate in India from 750,000 to 1,500. The continuing importance of this activity is borne out by the recent reappearance of more than a million cases of malaria in Ceylon where spraying was discontinued several years ago and by the persistence of thousands of cases in those few parts of India where the eradication program was handicapped by local inadequacies in the supply of DDT.

Food production. In considering public health benefits of pesticides, attention should also be called to the role of these chemicals in bringing about increased production of food. The need for increased food production to feed the expanding population is evident from the fact that malnutrition and starvation are among the most urgent world public health problems.

Other benefits. Control of certain species of pest insects, such as houseflies, cockroaches, and various innocuous mosquito species, contributes, if not specifically to public health, at least to a sense of well-being. Similarly, use of pesticides in control of Dutch Elm disease and hemlock looper has aided in the preservation of these shade trees and thereby enhanced the esthetic quality of our environment.

Hazards of Pesticides

Although chemicals provide effective and practical control of disease vector-bearing and crop-destroying insects, the necessity of using these toxic materials on man or on his immediate environment has created potential hazards that are of great public health significance.

Useful information on the effects of pesticides on human health may be obtained from use experience data, accidental poisoning cases, and human volunteer studies. Indirect data which can be extrapolated to apply to man with varying success can be obtained from studies with laboratory animals.

Use experiences. In manufacturing, formulating, packaging, and applying a pesticide, a number of workmen will receive significant exposure. It has been pointed out that, on the average, poisoning can be expected to appear most quickly, most frequently, most diversely, and most severely in those persons most extensively exposed (1). For this reason, the study of men with prolonged occupational exposure to

pesticides is of particular interest. However, the general population, exposed to small quantities of these chemicals as a residue in the diet or elsewhere in the environment, represents by far the largest group for study. Study of the general population is complicated by the lack of an unexposed or less-exposed control group for use as a comparison.

Health effects. Derivation of meaningful information on the health effects of pesticides from accidental poisoning cases and use experience data is dependent upon determining the exposure level involved and establishing that a toxic effect did or did not occur.

Studies of highly exposed workers are extremely useful in expanding our knowledge of the effects of pesticides in man. Ideal subjects are those workers whose exposure is limited to a single compound.

Extensive studies on workers who have occupational exposure to pesticides are now underway in contract studies being carried out by the Division of Pesticide Community Studies, FDA. There are 15 of these community study projects in areas of heavy pesticide usage throughout the United States. As one part of their contract, each project is asked to compile pesticide exposure and medical records of about 100 selected, high-exposure individuals. A group of individuals with minimal pesticide exposure serves as control. Results are now beginning to be derived from some of these studies. For example, Davies and his coworkers (4) from the Dade County, Florida project have shown changes in the phosphorus reabsorption index in exposed worker groups which they consider to be suggestive of renal tubular dysfunction. More recently, these same investigators have noted biochemical differences, including increases in serum glutamic oxalic transaminase (SGOT), alkaline phosphatase, serum osmolality, creatinine, and circulating amino acids in groups of workers with high pesticide exposure (15). The significance of these differences (that is whether they represent a beneficial adaptation or a detrimental effect) is not clear at this time.

In the WHO Malaria Control Campaign, no symptoms of DDT poisoning have been observed among the sprayers or among the inhabitants of the sprayed areas which numbered respectively 130,000 and 535 million at the peak of the campaign reported by the World Health Organization (16).

Exposure to DDT or other chlorinated hydrocarbon pesticides can be measured by determination of the compound or metabolites in fat or in blood. DDT storage in human fat has been known since 1948 when a single analysis showed 7 ppm.

Surveys. The first general survey for DDT was carried out in 1950 by Laug et al. (11). They demonstrated a mean DDT residue of 5.3 ppm in the fat of 75 persons with no special occupational exposure.

Since the 1950 study by Dr. Laug and his coworkers, a number of surveys have been conducted in various areas of the country to define the DDT storage level more exactly and to study its changes with time and geographic location. The results show that DDT is found in practically everyone in the general population of this country. The present mean storage level is about 2 ppm for DDT and about 6 ppm for metabolites of this compound, giving a total of approximately 8 ppm of DDT derived material. Recent studies have shown that race, geographic location, and age are all important factors in determining the DDT storage level for an individual. However, none of these factors seemed to influence the dieldrin storage level. There has been no significant increase in the storage of DDT by the general population of the United States since it was first measured in 1950. Studies by Hayes et al. (8) of volunteers have shown that the excretion of DDT is very slow in man. Thus, any decrease of DDT in food or other environmental media would be only slowly reflected in decreased fat storage levels of the compound.

Other chlorinated hydrocarbon pesticides in addition to those derived from DDT which are stored at detectable levels in body fat of the general population of this country include the beta isomer of benzene hexachloride, dieldrin, and heptachlor epoxide, all of which are present at mean levels below 1 ppm. The sensitive technique of electron capture gas chromatography has also made possible measurement of these compounds at the very low (ppb) levels at which they occur in blood in the general population.

Studies in experimental animals. Three problems of potential adverse health effects on man have been posed by recently reported studies carried out in experimental animals.

Teratology from 2,4,5-T formulations. In a contract study of various pesticides and related compounds for teratogenic effects, Courtney et al. (3) reported embryotoxicity from 2,4,5,-T. These effects were evidenced by statistically increased proportions of litters affected and by increased proportions of abnormal fetuses within litters. In particular, cleft palate and cystic

kidneys were significantly more prevalent. Effects were noted in both mice and rats. More recent work by Emerson et al. (5) and by Sparschu et al. (12) have indicated that a contaminant (2,3,7,8-tetrachlorodibenzo-*p*-dioxin) which was present at about 30 ppm in the 2,4,5-T formulation tested was highly toxic to experimental animals and produced terata at very low dosage. However, highly purified 2,4,5-T has also produced teratogenic effects in both hamsters and rats. Current research is aimed at determining the amount of the contaminant dioxin in commercially available formulations of 2,4,5-T, at defining more precisely the minimum dosage levels at which pure, 2,4,5-T and the dioxin contaminant produce significant teratogenic effects, and in determining if this dioxin or other related impurities are present in other pesticides containing the chlorophenolic moiety. Use restrictions have been placed on 2,4,5-T as a protection for the consumer against the possible teratogenic effect.

Carcinogenic hazard of DDT. Although earlier studies of the carcinogenic effect of DDT had yielded generally negative results, two recent studies in experimental animals suggest that DDT may be a potential carcinogen. In a screening test of 130 pesticides and related chemicals carried out by Innes et al. (9) under a contract with the National Cancer Institute, 10 compounds, including DDT, which are registered for use as pesticides, produced significantly increased incidence of tumors in hybrid mice. A number of other pesticide chemicals produced smaller increases in tumor incidence. It should be emphasized, however, that the study (9) was designed as a screening test to identify as many as possible of the carcinogenics submitted to it. The procedure detects a capacity for carcinogenic effect in the experimental animal. It does not define "no effect" levels, the existence of which is debated, nor does it predict the response of man either at the dosage levels tested or at the levels encountered by man in his environment. The procedures maximized the possibility of producing cancer in the test animals by use of tumor-susceptible hybrid strains of mice, by administration of very large dosages of toxicant and by use of young (neonatal) animals and continuation of dosage throughout the animal's lifetime.

In a separate study in mice extending over five generations by Tarjan and Kemeny (13), a dietary level of 3 ppm DDT produced a greater incidence of leukemia and malignant tumor beginning in the F_3 and F_2 generations, respectively, and continuing in the later generations.

Induction of drug metabolizing enzymes. In studies in various species of experimental animals, including rats and monkeys, it has been shown that exposure to DDT, chlordane, and other chlorinated hydrocarbon pesticides stimulates the activity of drug metabolizing enzymes localized in the liver microsomes. Experimentally this effect has been shown by a shortened sleeping time in response to a standard dosage of barbiturate. The effect of this enzyme induction in relation to reduced egg-shell thickness in birds has been implicated by a number of investigators in the etiology of decreased populations of certain species in areas of high pesticide usage. This effect is apparently mediated by an increased metabolic breakdown rate of the steroid cortisol in pesticide-exposed birds. Similar steroid related effects have apparently not been reported in man, although increased steroid metabolism has been noted in association with enzyme stimulation in rats. However, it has been noted that, in some instances, enzyme induction produced by concomitant drug therapy has caused tolerance to a desired therapeutic effect of an administered drug. For example, Goss et al. (6) have shown that phenobarbital administration significantly increased the required maintenance dosage of bishydroxycoumarin by patients receiving long-term anticoagulant therapy. Kolmodin et al. (10) reported increased rate of metabolism of foreign chemicals in workers having occupational exposure to chlorinated hydrocarbon pesticides. They also demonstrated a decreased plasma half-life of antipyrine in pesticide spraymen as compared to a control group.

The microsomal enzyme inductive effect of DDT has been utilized therapeutically by Thompson et al. (14) who treated a case of familial unconjugated nonhemolytic jaundice with DDT. The patient was given orally 90 mg DDT per day for 6 months. His plasma bilirubin became normal soon after treatment was begun and remained normal during 7 months after cessation of DDT dosage. No side effects were noted.

On the other hand, drugs may also influence pesticide metabolism. Davies et al. (4) reported lowered blood levels of DDE in patients taking the anticonvulsant drugs phenobarbital and diphenylhydantoin.

Human volunteer studies. Certain information on the toxicology of pesticides can be obtained only through studies on volunteers. To be sure, volunteers are generally restricted to lower dosages than those actually encountered in use, and there are practical limitations on the

duration of studies. However, work with volunteers makes it possible to study the relation of absorption, storage, excretion, and physiological effect to an accurately known dosage. Some physiological functions, such as reaction time, visual acuity, and ability to judge distance, can be studied in animals only with so much difficulty that the results are hard to interpret even for the species under study.

Our organization has primarily been involved in study of DDT in volunteers by Hayes et al. (7, 8). Ninety men were involved in the project. The subjects were divided into three groups, which received oral doses of DDT dissolved in corn oil at doses of 0, 3.5, and 35 mg per man per day for up to two years. The last two doses were about 20 and 200 times the ordinary dietary level of DDT. The highest dose chosen was about one-fifth of that estimated to cause transient mild sickness, based on animal experiments and on the smallest single acute dose known to produce mild illness in man. No clinical effect associated with DDT dosage was detected by the men themselves or by careful physical examination and laboratory testing. The storage of DDT in body fat was proportional to the dose. About one year was required for the men to reach equilibrium of DDT storage. Following this time no increase in DDT storage occurred, although the men remained on the dose for an additional year. The loss of DDT from body fat storage was quite slow.

Summary

In their recent report, the Commission appointed by Secretary Finch to examine the relationship between pesticides and environmental health emphasized three broad principles related to pesticide usage:

1. Chemicals, including pesticides used to increase food production, are of such importance in modern life that we must learn to live with them.

2. In looking at their relative merits and hazards we must make individual judgments upon the value of each chemical, including the alternatives presented by the nonuse of these chemicals. We must continue to accumulate scientific data about the effects of these chemicals on the total ecology.

3. The final decision regarding the usage of these chemicals must be made by those governmental agencies with the statutory responsibilities for the public health, and for pesticide registration.

The Commission also listed a number of specific recommendations for implementing these principles. In accord with these recommendations, restrictions of use are currently being imposed on DDT and DDD, 2,4,5-T, and the alkyl mercury compounds used as seed treatments. Use restrictions are also under review for a number of other persistent pesticides, including aldrin, dieldrin, endrin, heptachlor, chlordane, BHC, lindane, and compounds containing lead, arsenic, and mercury. These actions represent significant progress in the control of pesticide hazards.

For the future, it must be remembered that many people are genuinely concerned over the widespread occurrence of low amounts of these chemicals in our environment, in wildlife, in domestic animals, and in man himself. There is no doubt that the widespread finding of small quantities of pesticides or breakdown products or both in these various media is disquieting. Similarly, the detection of a carcinogenic or teratogenic effect on experimental animals from a pesticide chemical indicates a potential hazard of the chemical for man. However, I believe that it is important that these amounts be considered quantitatively. Dosage is the single most important factor determining toxicity, including cancer and embryotoxicity. Any chemical can become toxic provided that it is administered at a high enough dosage rate. In extrapolating from laboratory animal studies to practical hazard to man, the toxicologist must evaluate other factors, in addition to dosage, which determine the relative severity of the test, such as route of administration, formulation, and age of the test animals. It is also important to note that analytical chemical techniques which are currently available for measuring environmental contamination and human exposure are extremely sensitive. Increased attention must now be given to determining and to interpreting biochemical, physiological, and pharmacological effects on experimental animals and man so that the human health significance of these low-level environmental exposures to pesticides can be adequately evaluated.

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TOXICOLOGY PROGRAM
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HEALTH SURVEY OF PEST CONTROL OPERATORS

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Any possible long-term, toxic effects of a compound are most likely to appear in persons with prolonged, intensive exposure. Pest control operators offer an opportunity for seeking the long-term effects of economic poisons because they handle a variety of these compounds in large amounts. However, a difficulty in studying these workmen is that they are often employed by small companies, and these companies are widely scattered. A second difficulty involves the necessity of surveying large numbers of people to find a possible increase in the incidence of diseases that occur infrequently.

These difficulties in making a survey of the health of pest control operators were overcome through the generous cooperation of the National Pest Control Association. Although the limitations of a survey based on questionnaires were clearly recognized, it was decided to undertake a pilot study. After members of the Association had voted for the survey, questionnaires to elicit the needed information were designed and in 1961 were distributed to member firms and their employees. The results obtained from analysis of the answers are of considerable interest; they revealed cases of acute poisoning, dermatitis, and allergy in persons with heavy direct exposure to pesticides, but failed to suggest the association of pesticides with any other disease.

Questionnaires

There were two basic questionnaires, one for recording company data and one to be filled in by individual employees. Both were revised several times to make them as complete and clear as possible. The staff members of the Association were responsible for seeing that the terms used corresponded to those in the industry and that chemicals used by the industry were properly listed. The medical questions were designed to elicit a record of any significant disease but to avoid causing apprehension.

Briefly, information was sought from each company regarding the number of personnel in different categories, the rate of turnover, and the rate of sick leave.

Each individual was asked about the duration and character of his occupation within the pesti-

cide industry, the formulations used, and the duration and intensity of his contact with 38 separate pesticides as well as others he was asked to specify. Inquiry was also made about use or neglect of eight protective devices and eight aspects of hygiene. Questions were asked about the age and state of health not only of the individual but of every member of his household including those who had died within the last 15 years. The nature of both present and past illnesses was investigated for all the living, and the cause of death for those who had died. The following directions for including diseases appeared below a table for listing the worker and his family:

> For each person above, list below any disease, other than colds, influenza, and childhood diseases not already explained in the table (for example: Mary, frequent, severe headache last 6 months; John, Jr., pneumonia, 1955, with complete recovery). Be sure to include any irritation of the skin or any other trouble known or thought to have been caused by pesticides or their solvents. If such trouble was caused by spillage or some other special exposure, say so. If significant disease was not diagnosed, give brief description (for example: Frank had fever and was in bed for about 2 weeks in summer 1957, but recovered).

It must be explained that workers generally recognize that some pesticides and solvents can cause dermatitis, so that mention of this matter as an illustration did not tend to bias the data on the one hand or cause apprehension of the worker on the other. It was hoped that the question about undiagnosed disease would bring out significant difficulties, no matter how obscure their identity or cause.

A sufficiently serious disease would remove an employee from the working force and would not be represented in a survey of personnel health. Relatives were included on the possibility that a wider range of diseases including serious ones could be observed among them.

After questionnaires were reviewed and coded by a physician, the information was transferred to IBM cards for data processing.

TABLE I
COOPERATION IN THE NPCA SURVEY OF HEALTH AND SAFETY

		Companies	Personnel	Relatives	Total Family
Total Association		957	6,000*		
Cooperators	Total	115	1,396		
	Forms made	115	1,145	3,141	4,286
	Forms used	114	1,105	3,083	4,188

*Estimated

TABLE II
PERSONNEL AND RELATIVES GROUPED ACCORDING TO JOB CLASSIFICATION

Category	Servicemen Personnel	Servicemen Relatives	Clerks Personnel	Clerks Relatives	Administrators Personnel	Administrators Relatives
Total Number	799	2,347	156	313	150	423
White	730	2,161	150	302	148	420
Negro	49	139	3	3	1	1
Race Unstated	20	47	3	8	1	2

Cooperation

Twelve percent of all companies represented by the N.P.C.A. responded. A little more than 20% of the servicemen and a little less than 20% of total personnel submitted completed questionnaires. Data from the forms of 1,105 personnel were used. There were 3,083 additional family members represented by these forms, making a total survey population of 4,188 (Table I).

The average member company employs 6.2 personnel. The average cooperating company employed 12.1 personnel, indicating that the response was better from larger firms.

Companies from 36 states participated in the study, ranging in number from one to 14 per state. Fourteen participating companies were located in New York, and 8 each in California and Texas.

Characteristics of Personnel and Relatives

Three exposure categories were used — servicemen, clerks and administrators — and in most instances the applicable category for an employee was obvious from the position title and the work description. Owner-operators in one to three man companies were classified as servicemen because, by necessity, they have extensive exposure to pesticides. Executives in larger companies were classified as administrators in spite of some exposure to insecticides. In some instances, assignment to a group depended solely upon amount of exposure to pesticides, irrespective of the name applied to the position.

All but one of the servicemen and all but eight of the executives were male. The only servicewoman mixed insecticides in a formulating plant. There were 25 males classified as clerks. The clerks included individuals who had no definite exposure to pesticides, and included male office workers and janitors, as well as female secretaries.

The population was predominantly white; only 53 employees, or less than 5%, were Negro. Other races were not represented (Table II). The mean ages of servicemen (37.7) and clerks (38.3) were similar, while the average age of administrators was 44.8, about seven years older.

The mean ages of the relatives of servicemen, clerks, and administrators were 19.7, 29.8, and 22.8, respectively. Approximately one half of the total family members were under 24 (Table III). The average age of the relatives of clerks was seven to ten years older than the ages for the other two groups because the clerks were more often single, living with parents. There were 112 individuals 65 and over, of whom only 22 were personnel and the rest were relatives.

TABLE III
AGE DISTRIBUTION OF PERSONNEL AND RELATIVES

Age Group	Number of Personnel	Number of Relatives	Total Number
0-24	137	1,943	2,080
25-34	312	347	659
35-44	285	263	548
45-54	215	181	396
55-64	104	123	227
65-74	21	60	81
75+	1	30	31
Unstated	30	136	166
Total	1,105	3,083	4,188

Company Data

As shown in Table IV, the use of sick leave was low, averaging three man-days per year or less for each category of personnel.

The average number of persons leaving per year (two per company) does not seem high. However, this amounted to 16.7% of total personnel each year (Table IV). The number of persons hired per year averaged 3.1 per company, indicating growth of the firms. Companies engaged in termite control had a greater turnover per year (21%) than the other companies (12%), a fact associated with the seasonal nature of termite control work. A part of the turnover in other companies may also be associated with seasonal jobs.

Exposure to Pesticides

By definition, all servicemen had exposure to pesticides and this was almost always extensive over a period of years. At least 83% of servicemen and 78% of executives had worked with pesticides for over one year (Table V). Administrators had fewer hours of exposure per week than servicemen and this exposure was often in a supervisory capacity. In some instances, administrators had no present contact with pesticides but had had previous exposure in other job capacities.

Thirty-three clerks stated that they had no exposure to pesticides (Table V). Seventy-nine others left this question unanswered but indicated on other parts of the questionnaire that they did not use pesticides in their occupation.

TABLE IV
COMPANY DATA

	Servicemen	Clerks	Administrators	Total Personnel
Sick Leave				
Man-days per year				
Average	3	3	1	
Range	0-16.5	0-10	0-5	
Turnover (No. leaving per year)				
Person per company				
Average	1.5	0.7	0.2	2.0
Range	0-9.4	0-4	0-1.2	0-12.1
Persons per 100 personnel				
Average	19.6	27.2	5.3	16.7
Range	0-150	0-200	0-100	0-102

In general, servicemen used a variety of compounds, particularly insecticides and rodenticides, as often as four to six days per week. All servicemen were exposed to chlorinated hydrocarbon and organic phosphorus insecticides. Almost all applied rodenticides, and the majority used botanical insecticides and inorganic materials. Fumigants and herbicides were used less often. DDT, chlordane, lindane, malathion, Diazinon, pyrethrum, and anticoagulant rodenticides were each applied by the majority of servicemen during the year prior to the survey. Each of the other 31 pesticides listed on the questionnaire was used by less than half of the servicemen.

Servicemen generally wore protective clothing and respirators or gas masks when needed, and most showered at the end of a working day. On the other hand, some desirable safety precautions were not available to many. Two hundred and nine of the servicemen used the same vehicle for work and for personal use, and 187 did not keep chemicals in a compartment separate from the driver's. A few of the servicemen indicated that facilities were not available for washing before smoking and eating or in case of an accident. Others reported that they did not usually wash after an accident (48) or before smoking (166) and eating (33), although facilities were available.

TABLE V
YEARS OF EXPOSURE TO PESTICIDES REPORTED BY PERSONNEL

Years	Servicemen	Clerks	Administrators
None	0	33	10
>1	106	1	2
1-4	278	22	19
5-9	172	9	26
10-19	146	9	30
20-29	44	3	23
30+	18	0	13
Not stated	35	79	27
Total	799	156	150

Illness Reported in Survey

All illnesses listed in the questionnaires were included in Tables VI and VII, except where minor illness, such as a cold, was reported in spite of directions to the contrary. The statistics for diseases in relatives (Table VII) include all deaths.

Appendectomies, herniorrhaphies, tonsillectomies and all other surgical procedures, except those for cancer, were included under surgery. It thus happened that such diseases as peptic ulcer requiring surgery could be listed twice. However, cancer was listed only once whether surgery was involved or not.

Illness was reported in 13.3% of personnel and in 9.1% of their relatives. This difference does not seem striking in light of the age difference between these two groups. Clerks reported more illness in their relatives than in themselves. A comparison of the relatives of different groups of personnel demonstrated a positive correlation between the average age of the group and the amount of illness reported.

Slightly over 14% of the servicemen but only 7% of the clerks reported illness. At least two factors contributed to this discrepancy — the difference in sex, and the fact that servicemen filled out the forms more carefully and completely than the clerks, who apparently felt that the questionnaires did not apply to them since they did not actually handle the pesticides.

The reports of acute toxicity, allergy, dermatitis, dizziness, headache or other effects due at least in part to pesticides were distributed among the different companies in proportion to their size. There was no evidence that the safety record was influenced by the size of the company.

Systemic Poisoning: There were 20 servicemen and administrators who reported toxicity due to pesticides (Table VIII). From the descriptions, three of these cases, all due to cyanide, seemed near fatal. In one of these, described as almost fatal, the symptoms were unspecified. In the other two cases, unconsciousness for a few minutes in one and for six hours in the other resulted from cyanide exposure.

In the other cases of pesticide toxicity, the symptoms specified were minor. Headache and dizziness were the most common complaints and were attributed to the toxicity of both chlorinated hydrocarbon and organophosphorus insecticides. No convulsions were reported as a result of toxicity to chlorinated hydrocarbon insecticides.

The companies were not asked if any deaths among personnel had occurred as a result of pesticide toxicity. However, a clerk reported that her husband, a former serviceman, died of poisoning due to methyl bromide.

Dermatitis: One of the few diseases that seemed to be clearly influenced by pesticide exposure was dermatitis. Personnel reported 13 times more dermatitis for themselves (2.7%) than for their relatives (0.2%). Fifty-four percent (14) and 66% (2) of these cases in servicemen and executives, respectively, were actually attributed to insecticides. In 12 of these 16 instances the etiologic agent was specified. Three cases were due to chlordane, two to methyl bromide and one each to pentachlorophenol, DDT and Diazinon, Diazinon, Korlan, and Deo-Base oil.

There were also two instances of chemical burns, classified as dermatitis, sustained by servicemen after spilling methyl bromide on their skin. One case of recurrent dermatitis in the wife of a serviceman was said to be due to exposure to lindane on the serviceman's clothes. There were no cases of dermatitis attributed to pesticides other than insecticides, but two servicemen contracted creeping eruption several times while crawling under houses.

Allergy: Asthma and hay fever were included in this category. The prevalence of one or both of these diseases was higher in clerks than in other personnel. No cases of asthma were reported by personnel; however, in some instances, the type of allergy was unspecified. Asthma was reported in six relatives of employees.

In contrast to dermatitis, the prevalence of allergy did not differ in personnel and relatives (personnel, 0.7%; relatives, 0.6%). Pyrethrum was specified as a cause of hay fever in one serviceman, and as the probable cause in the relative of a clerk who was exposed while riding in a company truck. Malathion aggravated the hay fever of a serviceman's wife. One serviceman suffered from an unspecified allergy which was aggravated by pesticides but not caused by them.

Other Illness of Personnel: As already stated, clerks reported less illness than other personnel (Table VI). Because they were predominantly young women, this might be expected for such diseases as peptic ulcer and cardiovascular disease but not for arthritis, for which the incidence is higher in women. The occurrence of most diseases was quite low in all personnel, and it may be that with a larger sample of clerks, cases of other diseases would appear in this group. The servicemen and administrators were similar as to the amount and type of disease reported.

There were two cases of cancer in servicemen. Both these men considered themselves to be in good health after surgery in 1960. Two servicemen reported pulmonary disease, one case of chronic bronchitis and one of hemoptysis of un-

TABLE VI
ILLNESS REPORTED BY PERSONNEL

Disease Category	Servicemen Cases	Servicemen Percent	Clerks Cases	Clerks Percent	Administrators Cases	Administrators Percent
No disease	685	85.7	145	93.0	128	85.3
Headache	14	1.8	3	1.9	3	2.0
Dizziness	5	.6			1	.7
Allergy	4	.5	3	1.9	1	.7
Arthritis	5	.6			3	2.0
Cancer	2	.3				
Cardiovascular	6	.8			1	.7
Dermatitis	26	3.3	1	.6	3	2.0
Diabetes	4	.5	3	1.9	1	.7
Gastrointestinal	12	1.5	1	.6	2	1.3
Infection (including pneumonia)	18	2.3			2	1.3
Liver	4	.5			1	.7
Pulmonary	2	.3				
Renal	4	.5			1	.7
Surgery	5	.6	2	1.3	2	1.3
Accidents	4	.5			2	1.3
Miscellaneous*	3	.4				
Health status unspecified	9	1.1			1	.7

*Mental symptoms, ophthalmological disease.

known etiology. Three of the five cases of renal disease reported by personnel were due to renal lithiasis. No case of renal disease was attributed to pesticides. There were no cases of chronic liver disease reported but there were five cases of liver disease all due to hepatitis in personnel.

Comparison of Employee Health with a Previous Report: The present data were compared with results from an earlier study of employees of a large chemical firm[1] (Table IX). That study included only male employees, so clerks were omitted from consideration in the comparison. The age range was similar.

As was expected, a lower incidence of illness was found in the present study. The primary explanation for this difference is that employees in the other study underwent physical and laboratory examinations, as well as examination through histories as in this study. Diseases that patients identify clearly were reported at about the same rate, whereas pathological conditions that would not be recognizable to the individual showed a lower incidence in this study. For example, heart disease in general was reported only about half as much in the present study, but the incidence of myocardial infarction, a type of heart disease an individual is almost certain to be aware of, was about the same in both studies (see Table IX).

A higher incidence of headache and dizziness was noted in the present study (Table IX). When symptoms due to recognized instances of pesticide intoxication were omitted, however, complaints of dizziness and headache decreased to 0.2% and 1.2%, respectively.

Other Illness of Relatives: Variations in type of illness reported for the relatives of different classes of personnel would be expected because of their dissimilarities in age and sex. The frequency of reported illness was generally lower in the families of servicemen than in the families of other categories of personnel (Table VII).

There was a relatively high rate of cardiovascular disease and less striking higher rates for other illnesses in the relatives of clerks. A prominent factor is the greater average age and the predominance of males in this group — 57% compared to 35% in each of the other groups of relatives.

Included under arthritis were several cases of rheumatic fever and one case of lupus erythematosus. Six individuals were classified as having congenital disease (two cases each of cerebral palsy and cystic fibrosis, and one each of congenital heart disease and mongolism).

Deaths Reported in Relatives: There were reports of 83 deaths over a period of 15 years in the relatives of personnel (Table X). Cardiovascular disease, including cerebral vascular accidents, was the leading cause, accounting for over one third of the deaths. Cancer was second as a cause of death. Only one death was attributed to pesticides, the serviceman who died of poisoning by methyl bromide.

It is difficult to ascertain the expected incidence of death for various diseases, since these deaths were reported for a period of 15 years. However, the distribution of these deaths was compared to that reported for the United States in 1959 (Table X). There is some variation that can be explained in part, at least, by the large

TABLE VII
ILLNESS REPORTED FOR RELATIVES OF PERSONNEL

Disease Category	Servicemen Cases	Servicemen Percent	Clerks Cases	Clerks Percent	Administrators Cases	Administrators Percent
No disease	2156	91.9	270	86.3	375	88.7
Headache	9	.4			2	.5
Allergy	13	.6	3	1.0	3	.7
Arthritis	13	.6	2	.6	2	.5
Cancer	12	.5	4	1.3	4	1.0
Cardiovascular	28	1.2	17	5.4	9	2.1
Congenital	5	.2			1	.2
Dermatitis	6	.3			1	.2
Diabetes	3	.1	1	.3	2	.5
Gastrointestinal	6	.3	1	.3	2	.5
Infection (including pneumonia)	37	1.6	5	1.6	4	1.0
Liver	1	.04				
Pulmonary	3	.1				
Renal	2	.1	2	.6		
Senility or Old Age	1	.04	2	.6	2	.5
Surgery	14	.6	5	1.6	4	1.0
Accidents and trauma	6	.3	2	.6	3	.7
Miscellaneous*	8	.3			2	.5
Death, Miscellaneous**	5	.2				
Health status unspecified	34	1.4	2	.6	10	2.4

*Non-surgical gynecological disease, Parkinson's disease, ophthalmological disease, mental symptoms.
**Neonatal—2; Unspecified—3.

discrepancy in the size of the two groups. There was a slightly greater proportion of deaths due to cancer and a lesser proportion due to diseases of circulation in the present study than in the United States as a whole. There was a striking discrepancy between this study and the national statistics for cystic fibrosis, a familial disease. However, both cases in this study were in the same family, and the difference can be explained by sampling variation.

There were three deaths due to diseases of the lymphatic and blood-forming organs (two cases of leukemia and one of Hodgkin's disease). In the case of Hodgkin's disease and in one of the leukemia cases, the employees started work as pesticide applicators after the disease was discovered in their relatives, who later died. There were no other diseases of the blood reported in the present study, either as deaths or as illness.

Comparison of Family Data with the National Health Survey: There are certain similarities between the present study and the National Health Survey.[2] Both include families and information may be supplied by one member of a family, although this was more often a female in the case of the National Health Survey than in the present study. The National Health Survey is based on a random sample and standardized interviews, and would be expected to show a higher incidence of disease than the present study.

It was necessary to compare age groups because of the difference in age of the two populations. The data from the two surveys could be compared for arthritis; allergy, including asthma; diabetes; heart disease; hypertension; and peptic ulcer. For each of these disease categories, the incidence was greater in the National Health Survey. The data for diabetes, however, was similar for the two surveys except in the older age groups, where the number of people in the present study was small.

TABLE VIII
PESTICIDE TOXICITY REPORTED BY PERSONNEL

Insecticide	Symptoms: Unconsciousness	Dizziness	Headache	Increased Secretions	Nausea	Nervousness	Weakness	Unspecified	Number of Cases
Chlordane		1	1					1	3
Cyanide	2						1	1	4
DDVP		1	1	1				1	3
Diazinon		2							2
Dieldrin								1	1
Korlan						1			1
Lindane	1*		1						2
Pentachlorophenol								1	1
Unspecified			3		2				3
Total									20

*Fainted while using lindane.

TABLE IX
COMPARISON OF SERVICEMEN AND ADMINISTRATORS WITH EMPLOYEES OF A CHEMICAL FIRM[1]

Disease	This Study Cases	This Study Percent	Previous Study Cases	Previous Study Percent
Total Number	949		27,718	
No Disease	813	85.7	16,719	60.3
Headache	17	1.8	195	0.7
Dizziness	6	0.6	81	0.3
Allergy	5	0.5	252	0.9
Arthritis	8	0.8	472	1.7
Cancer	2	0.2	51	0.2
Diabetes	5	0.5	130	0.5
Heart Disease — Total	6	0.6	378	1.4
Myocardial Infarction	(3)	(0.3)	(122)	(0.4)
Peptic ulcer	9	0.9	459	1.7
Pulmonary	2	0.2	189	0.7
Renal	5	0.5	191	0.7
Skin disease	29	3.1	1,623	5.9

TABLE X
CAUSES OF DEATH IN RELATIVES OF PERSONNEL COMPARED WITH U. S. — 1959*

Disease	This Study Number	This Study Percent	U. S. — 1959 Number	U. S. — 1959 Percent
Circulation	24	28.9	706,960	42.7
Cancer (incl. leukemia)	17	20.5	264,996	16.0
Leukemia	(2)	(2.4)	(12,270)	(0.7)
CNS — Vascular	8	9.6	191,376	11.6
Accidents	8	9.6	118,897	7.2
Respiratory system	4	4.8	79,631	4.8
Infections	4	4.8	24,629	1.5
Diabetes	2	2.4	28,080	1.7
Cystic fibrosis	2	2.4	590	0.04
Genitourinary	1	1.2	30,011	1.8
Congenital heart	1	1.2	11,021	0.7
Asthma	1	1.2	4,984	0.3
Arthritis	1	1.2	2,068	0.1
Others	10**	12.0	193,571	11.6
Total	83	100.0	1,656,814	100.0

*U. S. Public Health Service Vital Statist. U. S., 1959.
**Old Age—3, neonatal—2, surgery—2, unspecified—3.

Comment

The death of a serviceman and the severe poisoning of three other individuals, as reported through the questionnaires, emphasize the hazard involved in handling the more toxic pesticides. These four cases involved fumigants whereas some of the chlorinated hydrocarbon and organic phosphorus compounds were the cause of less severe acute poisoning. With these few but important exceptions, the data obtained in this survey indicate no reason to believe that exposure to pesticides has affected the health of personnel or their relatives to any significant degree. Similar conclusions have been reached in more intensive studies on limited numbers of individuals with occupational exposure to pesticides.[3] In addition to actual toxicity, the only diseases found to be related to pesticide exposure were dermatitis and two cases of hay

fever. There were also two cases of allergy aggravated by pesticides but not caused by them.

Review of the safety practices revealed some obvious deficiencies on the part of some personnel. Correction of these deficiencies might lead to an even better safety record.

Summary

A survey of pest control operators was made in 1961 to determine any possible long-term toxic effects of pesticides. The difficulties in surveying large numbers were overcome through the cooperation of the National Pest Control Association.

Personnel of member firms completed a questionnaire which included biographical, occupational, and medical data. The medical questions were designed to elicit a record of any significant disease in both personnel and their relatives. Each company submitted information on number of personnel, rate of turnover, and use of sick leave.

Questionnaires were completed by more than 1,100 persons, or about 20% of those represented by the National Pest Control Association. These individuals were employed by 114 of the Association's 957 member firms.

The sick leave use was low, averaging three days per year for servicemen. In most instances, servicemen and administrators had lengthy exposure to pesticides. Cases of acute toxicity, dermatitis, and two cases of hay fever were related to exposure to pesticides. Aside from these, which were not frequent and were serious in only a few instances, the health of pest control personnel and of their families did not seem to be influenced to any significant degree by pesticides.

Review of the safety practices revealed deficiencies on the part of some personnel. Correction of these deficiencies might lead to an even better safety record.

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CHAPTER 16

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ASSESSMENT OF ENVIRONMENTAL EXPOSURE TO PESTICIDES

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PESTICIDES PROGRAM
National Communicable
Disease Center

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The importance of insects as vectors of disease, as pests, and as destroyers of crops has long been recognized, and the necessity for their control has led to the development of increasing numbers of new pesticidal agents. There are some inevitable hazards that accompany the use of these toxic materials. Each year a number of deaths and many more illnesses of varying degrees of severity are attributed to pesticides. Some of the newer organic phosphorus compounds, particularly parathion, and a few of the chlorinated hydrocarbon materials, such as dieldrin, have caused occupational poisoning. Such incidents are usually the result of accident, use of the materials in a careless manner, or neglect or inability of workers to wear adequate protective clothing. The possible hazard to residents from contamination of the environment with pesticides is less well recognized, and fewer quantitative data are available.

In order to evaluate the health hazard involved when working with these toxic compounds, it has been of value to determine the amount of exposure that workers undergo while carrying out various jobs related to the use of pesticides. Other studies have involved evaluation of the potential hazards of pesticides to persons having environmental exposure to these agents. This latter group includes persons living in or near orchards or other agricultural areas whose homes may receive drift contamination each time a pesticide is applied to the cropland.

This paper will review some of the studies that have been done to evaluate the hazard from both occupational and environmental exposure to pesticides.

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In the usual course of manufacturing, formulating, packaging, and applying the pesticide, a number of workmen will receive significant exposure. It has been pointed out that, on the average, poisoning can be expected to appear most quickly, most frequently, most diversely, and most severely in those persons most extensively exposed (Hayes, 1960). For this reason, the study of men with prolonged occupational exposure to pesticides is of particular interest.

In the correlation of exposure data with toxicity data for all groups, the major problem involves determination of the exposure level. Clearly, demonstration of lack of harm to a certain individual or group is essentially meaningless unless some measure of the degree of exposure involved is available.

A number of methods have been developed for measuring the exposure of workers or of residents to pesticides (Durham and Wolfe, 1962, 1963). These methods may be divided conveniently into, first, the direct methods of measurement, and second, the indirect methods. The direct methods involve the use of some mechanism to trap the toxic material as it comes in contact with the subject during his exposure period. The amount of trapped toxicant as determined by chemical analysis, bioassay, or other method is then a direct measure of the exposure being studied. The indirect methods involve the measurement of some effect of the toxicant upon the exposed individual.

The direct method of measurement has been used in our laboratory to estimate exposure of workers to a number of pesticides while carrying out various activities (Batchelor and Walker, 1954; Culver et al., 1956; Batchelor et al., 1956; Quinby et al., 1958; Wolfe et al., 1959; Wolfe et al., 1961; Durham and Wolfe, 1962; Wolfe et al., 1963). The procedures have been described in detail and the results reviewed (Durham and Wolfe, 1962). One of our techniques involves application of absorbent alpha-cellulose patches at various locations on the sprayman's skin or protective clothing and use of a specially designed respirator.

The alpha-cellulose pads are absorptive and yet do not generally become soaked with spray during exposure. Similarly, the operator's skin does not ordinarily get wet to the point of run-off; so it is assumed in this connection that both pads and skin retain all the spray that impinges on them. These patches are left in place as the worker goes about his usual duties for a measured period of time, usually one or more complete spray cycles. Then, the patches are removed and transported to the laboratory for extraction. Chemical analysis indicates the contamination of the various body parts sampled.

The amount of pesticide that comes into contact with unprotected skin areas of spray operators can then be calculated. Usually, it is assumed that the average minimum clothing worn includes shoes, socks, long trousers, a short-sleeved open-necked shirt, and no hat, no respirator, and no gloves. It is, of course, realized that this is an empirical estimate and that some spraymen wear more and some wear less protection. Many spraymen wear a hat, gloves, and a light protective jacket. Less commonly, workers wear a respirator. The surface areas of the usually unclothed body parts are determined using Berkow's values for surface area (Berkow, 1931).

The total exposure is the sum of the dermal exposure of the usually unclothed body parts and the respiratory exposure. The calculations involved in using this procedure to determine the exposure of a workman spraying an apple orchard with parathion are illustrated in Slide 1.

One shortcoming of the pad technique is the necessary assumption that the pad area is representative of the entire body part being measured. A procedure that has been found useful, particularly for uneven body surfaces, involves the use of white cotton knit garments that cover the study area during exposure. Gloves have been used for measuing exposure of the hands, T-shirts for upper body exposure (particularly for estimating the amount of toxicant that penetrates outer clothing), and socks for foot exposure (particularly for determining the amount of pesticide that penetrates the shoes when one walks in wet cover crops in recently sprayed areas).

Another method of measuring skin contamination involves swabbing or rinsing the skin with a solvent that will remove the toxicant and then analyzing the rinse solution. This method appears to give a somewhat more accurate measure of dermal exposure than the procedures described above, especially where hands and other irregular areas are involved.

As an alternative to the use of absorbent pads in the respirator, approximate respiratory exposure may be determined from the concentration of the pesticide in air using an assumed or measured tidal volume and respiratory rate. In our experience, these two procedures give results for respiratory exposure that correspond reasonably well.

Studies have now been carried out in our laboratories using these direct methods of measurement to evaluate the exposure of workers in 22 different spraying or dusting activities. A total of 12 different pesticides have been studied in this work. Some representative results are shown in Slide 2. In each of the situations shown here and in all the others which we have studied, the respiratory exposure represents only a small fraction of the dermal exposure.

Exposure values derived in this way can also be used to obtain additional information. The total calculated exposure expressed as milligrams per kilogram can be compared with dosage levels that produce different degrees of injury in experimental animals. However, precise animal data are not usually available for respiratory toxicity. Therefore, a weighting factor should be used to take into account the more rapid and more complete absorption of respiratory as compared with dermal doses of toxicant. A factor of 10 has been adopted empirically for this purpose. The formula used for the calculation of percentage of toxic dose is shown in Slide 3.

The calculated values for fraction of toxic dose absorbed per hour are given in the last column in Slide 2. There appears for each given insecticide to be a significant variation in hazard depending upon the type of activity in which the worker is engaged. For example, indoor house spraying with DDT seems to be about 7 times as hazardous as spraying apples, or as outdoor house spraying with the same compound. Furthermore, the lower concentrations used in application of the more toxic materials may not be enough to compensate for their greater inherent toxicity. Even if the very dilute formulations were completely safe, one still would have to consider contamination by the dangerous concentrates during mixing.

Another procedure has recently been suggested (Smyth, personal communication) for determining exposure and, particularly, for studying the relative dermal and respiratory absorption of pesticides by exposed individuals. This more recent procedure combines direct and indirect methods of measurement as defined above.

The new procedure involves estimation of total absorption of the chemical from measurement of the compound or its biotransformation product(s) in the urine or other excreta. Respiratory absorption is assumed to be equivalent to respiratory exposure and is, therefore, total potential respiratory absorption. It is estimated on the basis of concentration in air of the chemical under study and of an assumed tidal volume and respiratory rate for the exposed individual or by other applicable procedure. Dermal absorption is calculated by difference between total absorption and potential respiratory absorption. The value obtained through use of this method should represent a minimal value for dermal absorption.

In preliminary work carried out at our laboratory, the above technique has been used to calculate the absorption of parathion by spraymen during actual orchard spray operation (Durham and Wolfe, 1963). For each sprayman the total parathion absorbed was based on total urinary excretion of

paranitrophenol for several days (until a nonsignificant excretory level was reached), after the single spray exposure under study. Respiratory absorption was considered to be equivalent to respiratory exposure and was calculated for the time the worker actually sprayed on the day under study by using the mean parathion respiratory exposure (0.019 mg/hr) as determined for airblast sprayers (Durham and Wolfe, 1962). In addition, the dermal exposure was estimated for each sprayman under his actual work conditions using the alpha-cellulose pad technique.

Some representative results are shown in Slide 4. For each of the 6 spray exposures shown here, as well as for the 11 others that we have studied in this way, a positive value was obtained for the calculated dermal absorption. The calculated dermal absorption in each instance was greater than the potential respiratory absorption. Dermal absorption represented, as an average, 86.7 per cent of the total absorption. However, dermal absorption represented only a small percentage (range 0.1 to 2.8, mean 0.9) of the dermal exposure. There was in general a rather good correlation between dermal exposure and dermal absorption. A plot of this relationship suggests that the correlation may be logarithmic rather than linear.

Let us now consider some indirect methods of measuring exposure and their application. Exposure to the chlorinated hydrocarbon pesticides can be estimated from the storage level of the compounds or of metabolite(s) in adipose tissue or in certain instances from excretion of biotransformation products in urine. Exposure to the organic phosphorus compounds generally can be determined by measurement of blood cholinesterase activity. Exposure to parathion and other organic phosphorus compounds, which on hydrolysis yield p-nitrophenol or one of its congeners, can be estimated by determination of these phenolic compounds in urine (Elliott et al., 1960). Although applicable to a restricted group of compounds, this test has proved to be a more sensitive measure of absorption than is cholinesterase inhibition (Arterberry et al., 1961). A urine test based on excretion of organically bound phosphorus would be desirable, since metabolites of this type are, of course, common to all the compounds in this group.

The chlorinated hydrocarbon insecticide that has been studied most carefully in regard to fat storage is DDT. It has been reported that the average storage in fat for the general population of the United States with ordinary dietary habits, with no occupational contact with DDT and with little or no environmental exposure to the insecticide, was 4.9 ppm for DDT and 6.1 ppm for DDE. Persons in the general population who did have appreciable environmental exposure to pesticides from drift from nearby fields or orchards showed a small but

statistically significant increase in storage for both DDT (6.0 ppm) and DDE (8.6 ppm) in comparison with those with no environmental exposure. Occupational exposure resulted in a much more marked increase in the storage of DDT-derived material. Persons who had had moderate occupational exposure within a year stored DDT at an average concentration of 14.0 ppm and DDE at 19.0 ppm. The storage values for these exposure groups are summarized in Slide 5. In another study, one worker with extensive occupational exposure showed 648 ppm of DDT and 434 ppm of DDE in his body fat (Hayes et al., 1958). One can conclude from this work that environmental exposures incident to living or working in or near areas of heavy application of DDT caused deposits only very slightly greater than those in persons without environmental exposure. People with occupational exposure stored more DDT-derived material than other people, and the rate of storage was generally proportional to the intensity and frequency of exposure. No adverse health effects of either environmental or occupational exposure to DDT were noted.

Ortelee (1958) conducted clinical examination and laboratory tests, including determination of DDA excretion, on a group of 40 men with intensive and prolonged occupational exposure to DDT. Estimates of DDT absorption in these men were made by comparison of their urinary DDA concentrations with concentrations obtained from human volunteers on known daily oral dosages of technical DDT. The results indicated that 26 of these men had absorbed DDT at a rate equal to or higher than that associated with an oral dose of dissolved DDT at the rate of 35 mg. per man per day. The men had been exposed at this rate for 0.5 to 6.5 years (mean, 3.5 years), but showed no ill effects as judged by medical examination, their own reports, or their work attendance records.

A number of surveys designed to determine the incidence of poisoning from the more toxic organic phosphorus pesticides have been carried out. Some of these studies resulted from complaints arising out of local situations in which insecticides were alleged to be the cause of illness in persons exposed unintentionally and only slightly, usually from small amounts of pesticide drift into their environment.

Surveys of this sort have been done in a number of areas having very high usage of pesticides, including Wenatchee, Washington (Sumerford et al., 1953; Hayes et al., 1957), the Delta Area of Mississippi (Fowler, 1953; Quinby et al., 1958), and Phoenix, Arizona (Ganelin et al., manuscript in preparation). Generally, the surveys involved determination of cholinesterase level and/or paranitrophenol excretion and symptomatology, and correlation of these values with degree of exposure to organic phosphorus insecticides. In each instance cases of acute poisoning were found in individuals

belonging to groups with heavy occupational exposure to the organic phosphorus pesticides. The degree of illness corresponded, as nearly as could be judged, to the degree of exposure. Men who had occupational exposure to parathion frequently showed some depression of blood cholinesterase activity even though they remained well. Illnesses resembling mild poisoning were not found to be more common among persons living in an agricultural community (including those in or adjacent to orchards) if they had no occupational or gross accidental exposure than among persons in non-agricultural areas where insecticides were not used. Although no effect on their blood cholinesterase level was demonstrated, it has been possible to measure the excretion of paranitrophenol in the urine of people whose only exposure to parathion resulted from their living near treated orchards (Arterberry, et al., 1961). The occurrence of even mild illness was always associated with greater exposure and with the excretion of the parathion metabolite at a much higher rate than that encountered by the environmentally exposed group.

It is apparent from the above discussion that a considerable amount of data are available on the magnitude of exposure of workers and residents to pesticides during application for agricultural or public health purposes. A smaller amount of information is available on the relationship of this measured occupational or environmental exposure to the development of clinical signs or symptoms of poisoning or of demonstrable abnormalities of physiologic function. There is a need for extending application of the presently available techniques for measurement of exposure to other compounds and to other occupational and environmental situations. There is also need for additional data on exposure correlated with physiological effect.

Slide 1: Dermal and Respiratory Exposure to Parathion for a Workman Spraying Apples

Body Part	Pad Location or Area Rinsed	Body Area (Sq. ft.)	Parathion Recovery (Mg./sq.ft./hr.)	Total Calculated Exposure (Mg./body part/hr.)
Face	Shoulders	0.70	5.9	4.1
Front of Neck "V" of Chest	"V" of Chest	0.16	2.4	0.4
Back of Neck	Back of Neck	0.12	5.6	0.7
Forearms	Forearms	1.30	6.3	8.2
Hands	Hands	0.87	---*	3.9
Total Dermal Exposure	----	3.15	---	17.3
Respiratory Exposure	Respirator	---	---	0.02

*Bag rinse measurement for hand area.

Slide 2: Exposure of Workers to Pesticides While Carrying out Various Activities

Compound	Activity	Exposure		
		Dermal (mg./hr.)	Respiratory (mg./hr.)	Total (Per cent of toxic dose/hr.)
DDT	Spraying Apples	206	0.12	0.12
DDT	Indoor House Spraying	1755	7.10	1.02
DDT	Outdoor House Spraying	243	0.11	0.14
Parathion	Spraying Apples	17.3	0.02	1.19
Parathion	Spraying Citrus	17.9	----	----
Parathion	Spraying Potatoes	4.7	0.01	0.32
Parathion	Dusting Potatoes	7.8	0.16	0.64
Parathion	Thinning Apples	8.4	0.06	0.61

Slide 3: Formula for Calculation of Exposure in Terms of Percentage of Toxic Dose

Percentage of toxic dose =

$$\frac{\text{Dermal exp. (mg/hr)} + (\text{Resp. exp. (mg/hr)} \times 10)}{\text{Dermal } LD_{50} \text{ (mg/kg)} \times 70} \times 100$$

Slide 4: Calculated Dermal Absorption of Parathion by Orchard Spraymen

Subject	Total Urinary Parathion Excretion (mg.)	Respiratory Exposure			Calculated Dermal Absorption	
		mg/hr	hrs. exp.	Total mg.	Amount (mg.)	Per cent of Excretion
1	0.67	.020	6.25	0.13	0.54	80.6
2	1.50	.020	7.25	0.15	1.36	90.7
3	1.49	.020	7.50	0.15	1.34	89.9
4	1.36	.020	7.75	0.16	1.20	83.2
5	0.51	.020	5.00	0.10	0.41	80.4
6	7.91	.055	13.75	0.76	7.15	90.2
Mean	----	----	----	0.24	2.00	86.7

Slide 5: Storage of DDT and DDE in Fat as Influenced by Environment and Occupation

Exposure	Number of Persons	DDT Storage (ppm)	DDE Storage (ppm)
Environmental	110	6.0 $\pm$ 0.26	8.6 $\pm$ 0.48
Occupational	30	14.0 $\pm$ 1.5	19.0 $\pm$ 2.2
General Population	61	4.9 $\pm$ 0.35	6.1 $\pm$ 0.42

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Visual Effects Accompanying TEPP-Induced Miosis

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Pilots and others have long recognized the miosis which is frequently a consequence of spraying tetraethylpyrophosphate (TEPP) dust by aircraft. This effect of TEPP often occurs without symptoms referable to any part of the body except the eyes. Parathion (O,O-diethyl O-para-nitrophenyl thiophosphate) may also produce miosis, but it does so less frequently, and when it does the eye signs and symptoms are usually accompanied by general, systemic illness. The reason for the difference in clinical effect is not entirely clear but probably involves, among other things, the difference in molecular weight and vapor pressure of the two compounds.

Various flying accidents have been blamed on the effects of organic phosphates on pilots.* Two complaints which are occasionally made by the pilots themselves involve an inability to judge distance and a sensation that things are darker than the time of day, the season, and the weather justify.

A study in 1953 of the visual fields of 15 pilots and 2 other persons before, during, and after occupational exposure to TEPP did not reveal any meaningful change. However, only one pilot in this series was available for study of visual fields at a time when he actually had miosis. A much greater diversity of tests conducted during miosis seemed to be required to explain the reported disturbances of function.

The dosage level in the eye required to contract the pupil to 1 mm. diameter was worked out in an intensive study of one volunteer at three dosage levels. The study served to establish techniques for conducting a battery of ophthalmological tests. Instillation of 1 drop (about 0.01 cc.) of 0.0125% TEPP and later of 1 drop of 0.05% TEPP produced no measurable effect. Instillation of 2 drops (about 0.02 cc.) of 0.05% TEPP produced slight miosis and a slight increase of near accommodation. Maximal miosis was produced by 2 drops of 0.1% TEPP, the pupils being fixed at 1 mm. diameter. A fourth drop did not cause further miosis or other observed change. Visual acuity (Snellen), peripheral fields (Ferree-Rand simplified

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*References 1 and 4.

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perimeter), depth perception (Howard-Dolman), color vision (Ishihara), and subjective perception all remained within normal limits. The near point as measured by the Prince Rule moved from a predosage distance of about 13 cm. to 3.8 cm. for the right eye and 4.5 cm. for the left eye.

The next logical course of investigation was to induce miosis in a number of pilot-volunteers. Six men with no previous exposure during the spray season in which the tests were made were selected from a group of commercial dusting pilots and their occupational associates by screening with a medical and ophthalmologic history followed by medical examinations.

The TEPP used in this experiment consisted of 40% tetraethylpyrophosphate and 60% related organic phosphates. Each drop (0.01 ml.) of 0.1% technical (40%) TEPP contained 0.009 mg. of technical TEPP in peanut oil. The maximum dose (2 drops of 0.1% into each eye) totaled 0.036 mg. For the average body weight of 83 kg., the maximum dosage rate was 0.0004 mg/kg.

For each dosage level, the volunteers were given batteries of tests at intervals of one hour. About one week elapsed between the different TEPP dosages. With the minor exceptions noted, each battery of tests consisted of the following 23 tests.

The first group of tests in each battery was performed with the Ortho-Rater † for far vision—(1) vertical phoria; (2) lateral phoria; (3, 4, 5) acuity, eyes together and separately; (6) binocular depth perception; (7) color vision—and for near vision—(8, 9, 10) acuity, eyes together and separately; (11) vertical phoria; (12) lateral phoria. A transilluminated Snellen chart and associated rheostat ‡ were used to make the following tests: (13) Bilateral acuity. (This was checked at the 20/20 level on all candidates with full power load in the chart-lamp circuit. Tests of more critical acuity were not in order because subsequent threshold tests required the use of the 20/20 test line, which was the only one homogeneously illuminated at various intensities.) (14) Threshold of light intensity required for reading. (Following the test of bilateral acuity, the light intensity was turned down by means of the rheostat until the volunteer could not distinguish the letters and then turned up until he could. The reading in arbitrary units, 135 for the entire scale, was recorded.) (15) Threshold of light intensity required for perception. (For the tests at the highest dosage level, 2 drops of 0.1% TEPP, the rheostat reading was also recorded at the first point at which the subject could distinguish the faint pinkish light in the chart, i.e., the threshold of minimum light perception. As the power delivered by the rheostat to the light circuit was reduced, the quality of the light changed from incandescent white to orange and then to a faint pinkish glow before disappearing entirely.) The Prince Rule and No. 3 Jaeger print card were used to test (16) accommodation for near vision. The Snellen chart and appropriate lenses held in the usual test frame were used to test (17) accommodation for far vision in respect to positive lenses; (18) accommodation for far vision in respect to negative lenses. A camera was used to record (19, 20) pupil size and reaction to light. (The eye was photographed in a darkroom with normal lighting. After adaptation in the dark for five minutes, the eye was again photographed.) The Hare perimeter was used to determine (21) field of vision. (Readings were taken for white on the vertical and horizontal axes of the perimeter.) The Schiøtz tonometer was used to measure (22) ocular tension. Blood was drawn from the ear to determine

† Bausch and Lomb Optical Company, Professional Model.
‡ Fisher Scientific Powerstat, Type 116, output range 135 volts.

(23) plasma and red blood cell cholinesterase levels, by use of a modification of the Michel electrometric procedure.[3] (Blood was drawn on two occasions before any TEPP was instilled into the eyes and again at the end of the last battery of tests at each dosage level.)

The results of the study are summarized in Table 1. Where there were

TABLE 1.—*Selected Ophthalmologic Measurements of Certain Functions of the Eyes of Pilots into Which TEPP Had Been Instilled**

Function	Condition of Test	Unit of Measure	Eye†	Dosage Level and Time After Dosage					
				1 Drop Peanut Oil (Control)		2 Drops 0.1% TEPP			
				Before Dose	After 1 Hr.	Before Dose	1 Hr.	2 Hr.	3 Hr.
Diameter of pupil	Illuminated	Mm.	L	5.4	4.6	4.5	1.9	1.9	1.8
	Dark	Mm.	L	6.7	6.6	6.5	1.9	1.9	2.0
Acuity	Minimum light to read Snellen 20/20	Rheostat units	B	33.3	33.2	29.7	35.5	32.7	33.0
Light perception	Minimum light (pink)	Rheostat units	B			12.9	17.8	17.2	16.4
Accommodation	Prince Rule	Cm.	L	13.3	13.3	12.3	6.1	6.8	7.9
	Snellen chart	Pos. diopters	B	1.58	1.62	1.92	2.25	2.46	2.42
		Neg. diopters	B	2.83	3.17	3.71	5.96	6.58	7.68
Acuity	Ortho-Rater, far vision	Ortho-Rater scoring units	B	10.8	11.8	11.8	9.5	10.2	10.0
			R	11.2	12.2	11.5	9.3	9.7	9.5
			L	11.2	11.5	12.7	9.8	10.3	10.7
	Ortho-Rater, near vision	Same	B	11.8	11.5	11.8	10.5	10.3	10.0
			R	12.2	11.0	12.5	10.0	10.0	9.7
			L	11.3	12.0	11.8	9.7	10.3	10.2
Depth perception	Ortho-Rater	Ortho-Rater units	B	6.7	5.3	6.5	6.2	5.8	6.3
Visual fields	Hare perimeter, horizontal	Degrees subtended	L	135.7	138.9	133.9	127.8	133.9	128.2
	Hare perimeter, vertical	Same	L	109.0	111.7	108.3	103.3	100.6	99.2
Ocular tension	Schiøtz tonometer	Mm. of Hg	R		19.3				16.5
			L		17.7				14.3

* Mean values from six subjects.
† Left eye, right eye, or both eyes, as indicated.

no notable differences in the two eyes, only data for the left eye have been given in the Table. Some tests which gave negative or normal results at all dosage levels have been omitted from the Table.

The production of maximal miosis, at least to the point of fixing the pupils, was considered one of the requisites of this study. Fixation of the pupils with concomitant effects was obtained consistently only with 2 drops of 0.1% TEPP spaced 30 minutes apart and not with a single drop.

Subjectively the maximum dosage caused mild headaches, sensations of pressure in the eyeballs or over the frons, slight burning of the lids, "running" or "stopped-up" nose, and a sensation that "things were getting darker." These symptoms passed their peak during the first or second hour. Four of the pilots stated, upon self-inspection in the mirror, that their pupils were not as small following the experimental exposures as they were following occupational exposure in the summer. One pilot believed that the experimental miosis was as severe as he had ever experienced in applying TEPP by airplane. The sixth man had had insufficient prior exposure to make a significant comparison.

At the highest dosage level, the subjective complaints of reduction of light perception were corroborated by the Snellen chart light-threshold test

and also by the minimum perception of light in the same back-illuminated chart.

The Prince Rule test showed greatest accommodation for near vision at the one-hour observation battery (30 minutes after the second drop). The lens test for far accommodation revealed a gradually increasing accommodation, particularly to negative lenses, at least until the third hour. One of the subjects was tested at the fifth hour also and was found to have undergone no further change in this respect. The changes in accommodation may be accounted for, at least in part, on a physical basis. The accommodation for near vision and for far vision with negative lenses is associated with the increased convexity of the lens of the eye as well as with the greater depth of focus which accompanies constriction of the pupil. The accommodation for far vision with positive lenses can be explained by the greater depth of focus which accompanies constriction of the pupil.

According to the Snellen measurement at the usual illumination, no change of acuity occurred at any dosage. But, as suggested above, some persons, after the 2-drop dose of 0.1% TEPP, noted that they required more intense illumination of the chart in order to achieve the same 20/20 acuity which they had before dosage, whereas, with the test conducted at unvaried illumination intensity, the Ortho-Rater showed a definite loss of acuity at the highest dosage level, averaging about 2 scoring units from 12 to 10 (Snellen equivalent of 20/17 to 20/20 for far vision), for both eyes and for each eye separately at both near and far vision. This slight loss of acuity was most evident during the period (one hour after dosage) when the patients were complaining most of the effects of ciliary spasm, conjunctivitis, rhinitis, and headache. It is quite possible that the chemical irritative effects as well as the diminished light intensity inherent in the miosis may have contributed to this slight loss of acuity.

Depth perception was not changed significantly at any dosage as measured objectively or by subjective complaints.

TABLE 2.—*Ocular Tension in Millimeters of Mercury as Determined by Schiøtz Tonometer Before and After 0.1% TEPP*

Case No.	1 Hr. After Peanut Oil		3 Hr. After TEPP	
	Right	Left	Right	Left
2	19	19	13	13
3	26	17	28	17
4	17	20	16	15
5	25	20	17	15
7	13	13	12	12
9	16	17	13	14
Mean	19.3	17.7	16.5	14.3

Three hours after the administration of 2 drops of 0.1% TEPP, the average ocular tension of the six men dropped 2.8 and 3.4 mm. of mercury in the right and left eyes, respectively, as compared with normal levels established after instillation of peanut oil. The changes are summarized in Table 1 and given in more detail in Table 2. The tension of one man was a high normal after peanut oil and showed a paradoxical rise after only 1 drop of 0.1% TEPP. After the completely separate test with 2 drops of the same concentration, his tension was found to be back to his high normal level, and this same high normal level was still present one month after the last instillation of TEPP.

The averages of the tests for vertical and lateral phoria at near and far vision varied little. However, each of the subjects showed what appeared to be significant shifts in lateral phoria, but not all in the same direction.

Erythrocyte and plasma cholinesterase level, color vision, and perimetry remained normal throughout the entire experiment.

In order to be sure that the effects of the experimentally induced miosis were essentially the same as those of miosis acquired under conditions of actual application of TEPP dust, two pilot volunteers were reexamined during the season of occupational exposure. The rechecks were performed two to two and one-half hours after one pilot applied 2800 lb. of 1% TEPP (plus 1.5% other ethyl phosphates) dust and the other pilot applied 4900 lb. of the same formulation. One pilot showed no notable differences in the test results after the occupationally acquired miosis as compared with results after experimentally induced miosis. The second showed a greater ability to accommodate as measured by negative lenses at the usual Snellen test distance of 20 ft. His ability to read 20/20 was maintained up through − 7.00 D. compared with — 4.50 D. when his miosis was experimentally induced. However, as measured by the Prince Rule, accommodation was less than when miosis was induced. This second pilot also complained of loss of acuity in the right eye only ("has a shade over it" or "things look fuzzy"). The Snellen chart showed no detectable loss of acuity in this right eye, but the Ortho-Rater indicated a drop from his level with induced miosis of 10 to 4 scoring units (Snellen equivalent 20/20 to 20/50) for far vision. The left eye maintained the same acuity of vision after miosis was produced experimentally and occupationally. His acuity for near vision in the right eye dropped even farther after occupational exposure, from a normal of 10 scoring units to 1 unit (Jaeger equivalent: 1 to 10). The reason for this wide difference of results in the two methods of measurement is not yet apparent. It is believed that the repeated loss of acuity in the right eye of this particular pilot indicates a visual defect peculiar to his optical system.

By means of the several studies described thus far, physical explanations were found to account for all the predicted and recognized effects of TEPP in the eye. The one complaint by operating pilots remaining to be explained was their inability to judge distance with self-assurance. Dr. George H. Henton, Ophthalmologist, of Portland, Ore., who reviewed the results of the tests, suggested the possibility that radically unequal accommodation due to the production of miosis in one eye only might produce such effects. This hypothesis was consistent with clinical experience with patients who are placed on unilateral miotic therapy for the first time and also consistent with the infrequency of the inability to judge distance among pilots experi-

encing miosis after commercial applications. Moreover, several instances of unilateral miosis were discovered among pilots who were recently exposed as well as in old records of exposures.

As a test of this hypothesis, the first volunteer in whom bilateral miosis had been produced was retested with unilateral miosis following instillation of 2 drops of 0.1% TEPP. All ophthalmic results following unilateral induction were essentially the same for the single treated eye as they were for each eye following bilateral treatment. However, this volunteer did feel a little uncertain in going down or climbing stairways for about 12 hours after the instillation.

Six more nonpilot volunteers were given abbreviated testing after induction of unilateral miosis in the left eye. The objective findings were essentially the same (for the treated eye) as were those for the six pilots described earlier, but the volunteers with unilateral miosis had subjctive complaints for about 24 hours after the induction. Four of the subjects had no idea what minor disturbances of vision might occur. Because their subjective complaints are not easily subject to classification or quantitation, they are listed here.

CASE 1.—"Indefinable obscuring in the left field of vision and sensation that the two eyes were not on the same plane vertically."

CASE 2.—"The ground is coming up at me." "I feel one-sided." (The morning after induction, this volunteer hit his thumb three times in 20 minutes while attempting to nail fruit boxes. He has done this work for three months before and two months after this incident without such errors of distance judgment.)

CASE 3.—"The pegs are blurred" (on Howard-Dolman, but performance normal). "I feel like I'm stepping farther than I'm actually going. I'm giddy yet this morning." (This patient felt sweaty, especially on the back of his legs, about one and one-half hours after the first drop of TEPP. He was slightly nauseated and had tightness in his chest. He was nauseated by odor of ether while passing recovery rooms. This patient had been treated previously for neurocirculatory asthenia.)

CASE 4.—"It feels like it [the eye] is hanging out." "I feel like my left eye is wide open: it is bigger than my right eye and yet it feels like it does no good to look through the left eye." (This man missed the first step when reentering his home after the test.) "On the next afternoon I had the feeling that my left eye stared straight ahead, wide open and saw nothing. However, when I close my right eye, the image in the left looks O.K."

CASE 5.—"It feels cockeyed after the second drop." "I fumbled the sugar bowl, while removing it from a shelf at head height. I almost dropped it and I spilled sugar."

CASE 6.—"I have a vague feeling of not seeing too well." (This volunteer missed a step and almost fell.)

Thus, all seven of the volunteers in whom unilateral miosis was induced complained of subjective inability to perceive distance properly with self-assurance or experienced fumbling, stumbling, or other sensorimotor accidents or both.

Similar complaints frequently occur among ophthalmological patients in whom unilateral mioses is induced for therapeutic reasons. Dr. F. W. Jobe, of the Bausch and Lomb Optical Company, pointed out that these results are doubtless physiologically the same as the Pulfrich effect described by Duke-Elder [2] and in other textbooks. The Pulfrich effect causes the subject with unequal light intensities in the two eyes to perceive moving objects falsely; thus a pendulum appears to rotate in an ellipse instead of in one plane.

The induced or occupationally acquired miosis lasted from 12 to 24 hours, as indicated by the failure of the pupil to react to light and in accommo-

dation. Subjective complaints lasted about the same length of time. Partial constriction of the pupil lasted from two to three days.

Summary and Conclusions

Pilots and others have long recognized the miosis which is frequently a consequence of applying tetraethylpyrophosphate (TEPP) dust by aircraft. Accompanying the miosis, operating pilots have regularly noted a decrease in light perception and have more rarely experienced an inability to judge distance.

Two drops of 0.05% TEPP instilled into each eye of volunteers produced slight miosis and a slight increase of near accommodation.

Two drops of 0.1% TEPP instilled into each eye of volunteers produced maximal miosis, an increase in near and far accommodation, and a decrease in light perception but no inability to judge distance.

Two drops of 0.1% TEPP in only one eye of each of seven volunteers produced unilateral miosis and other expected changes in the treated eye but also caused all the volunteers to complain of difficulty in vision; four of the volunteers complained specifically of difficulty in judging distance, and six of them made sensorimotor errors of fumbling, stumbling, or other clumsiness.

It is concluded that infrequent unilateral contamination of the eye by spillage or other accident, accounts for the occasional inability of pilots applying TEPP to judge distance adequately. The incoordination which may accompany such inability to judge distance may be a serious threat to the pilots.

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